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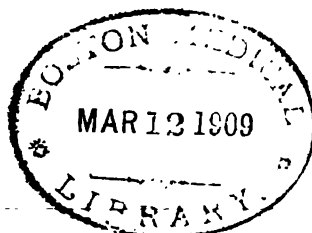
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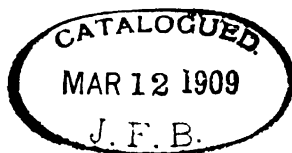
VOL. CXXXVI



PHILADELPHIA AND NEW YORK  
LEA & FEBIGER  
1908



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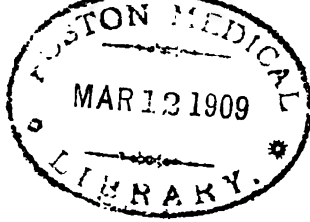
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JULY, 1908.

ORIGINAL ARTICLES.

**CONGENITAL PYLORIC SPASM AND CONGENITAL HYPERTROPHIC STENOSIS OF THE PYLORUS IN INFANCY.**

By HENRY KOPLIK, M.D.,

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THERE is no disease of infancy and childhood which, in the past five years, has attracted more attention than the so-called congenital stenosis of the pylorus, or, as it was formerly and is still called, congenital spasm of the pylorus. New methods of diagnosis, and the bad results of feeding in these cases seem to have brought about a more frequent recognition of the condition than formerly. When Beardsly described his case very little was thought of it, and apparently the condition was allowed to pass unrecognized. The publication of Landerer, in 1879, and that of Maier, in 1885, caused renewed discussion of this condition. Landerer described some autopsies in adult subjects, some of them having lived until the forties, which showed postmortem a narrowing of the pyloric orifice of the stomach. The history of these cases showed that they had suffered from infancy and childhood and during adult life from the effects of this stenosis.

Hirschsprung, in 1887, communicated two cases of pyloric stenosis occurring in infancy, both of which were fatal, the pylorus in both being considerably thickened, to the extent of not permitting even a small sound to be passed. In one case the pylorus resembled a tumor, and an examination showed a thickening of the longitudinal as well as the circular muscular fibers. Since this time many additional cases of this condition have been reported, so that I am convinced it can no longer be classed among the rare disorders occurring in infancy.

With all the observers who have seen these cases and discoursed upon them, there has arisen a difference of opinion which is not only confusing but disquieting. Some have criticised the observing capacities of others who have published their cases, and discussions have become almost personal in their nature. Especially violent was the discussion after the publication of the surgeon Stern, who was the first to operate in these cases when they appeared to him to be hopeless in their nature. The discussion of his case and the interchange of published letters between the surgeon and Pfaundler are now a matter of record. I shall not enter into this part of the subject, but simply state that Pfaundler's position can be explained by a possible difference in material.

I shall endeavor to show in this paper that this is a disease which is rather vacillating at times in its symptomatology; that the men who insist that the patients get well spontaneously are correct when their material is analyzed, and that those who insist on operative procedures in certain cases might be correct if their material is analyzed in a like manner. Both parties are possibly correct, but they have both been looking at opposite sides of the shield. It is for this purpose that I have decided to publish my own cases and critically analyze them in detail with an endeavor to introduce some clearness into the subject obscured by useless, and to me purely academic, discussions.

I may be pardoned if, for the sake of completeness, I go lightly into the symptomatology of an affection which has been so widely considered. As a rule, in cases of spasm or congenital stenosis of the pylorus the children are born perfectly well; the great majority of them have been breast-fed; I should say from the literature that fully two-thirds of the children were breast fed from the start. After a while, varying from one to four days, in other cases seven days, and in a great many cases the third week after birth, in exceptional cases the eighth week after birth, the vomiting begins. In a few cases, as in some of my own, there is a history that an attempt was made to feed the baby, in addition to the breast, on the bottle, and in these cases the vomiting began from the attempts at mixed feeding. In other cases there is no such history, the mother's milk being the only food; the milk seemed to be abundant, and there was no change in the milk or in the mother to account for the disturbance in the child. The vomiting occurs at first at intervals throughout the twenty-four hours, and soon becomes persistent, the child rejecting sometimes a portion or all of every nursing. Sometimes the history will show that the infant has rejected more than it had taken. This is quite characteristic, and points toward a retention in the stomach of some of the previous feedings. With the vomiting there is a steady emaciation or a stationary weight. If the weight is stationary, the patient is fortunate. If the emaciation is progressive, we see in a few weeks an infant which had been perfectly well at



birth, weighing the normal or above the normal, reduced to a distinctly marantic condition. With the vomiting there are other signs of constitutional disturbance. It seems that every time the breast is given to the child, or within a few minutes after nursing, there are evidences in some cases of pain; the children will cry, and this will be told spontaneously to the physician by the mother. In addition there is constipation in most cases, or the movements are small, minimal in quantity, sometimes fluid in consistency, or they may be greenish. As a rule, the movements indicate that very little has passed through the gut. Physical examination in these cases reveals in the vast majority of instances a characteristic condition of the surface of the abdomen. On the introduction of food there is a peristalsis visible to a greater or less extent on the surface of the abdomen. This peristalsis begins underneath the left costal border, passes forward to Traube's triangle, and there seems to stop, being interrupted by a sort of groove, and is taken up again by a second wave of peristalsis which passes onward beyond the ensiform cartilage, then downward, and disappears. Some authors have described a reverse peristalsis just previous to vomiting, but I could never convince myself of the fact, possibly because I have not seen these particular cases. If there is a reverse wave of peristalsis, it must be instantaneous, and I have not yet observed it. Ibrahim also expresses his lack of information on this reverse wave. In some cases I have seen the peristalsis so extreme that just previous to vomiting the stomach would in a manner erect itself on the abdomen and divide itself distinctly from what appears to be the pyloric end of the stomach; it would contract, and then the vomiting would take place.

The vomiting is projectile in its nature, as if there was a sudden violent contraction of the stomach and a forcing upward of the contents. In some cases careful examination during this period of contraction and peristalsis reveals a small hard nodule, cartilage-like in consistency, situated sometimes beneath the liver or its border and running directly downward toward the umbilicus. This structure, situated deeply against the vertebral column, is undoubtedly the pyloric end or valve of the stomach as it meets the duodenum.

Some authors like Ibrahim have described singultus in these cases, and also eructations of gas, but inasmuch as these are quite common in healthy breast-fed infants, it seems to obscure the picture by laying any stress upon them.

The peristalsis which I have described is present in a majority of cases, but it is not necessarily an accompaniment of all of them. It is sometimes entirely absent during the height of the affection, and is only seen at times. The pylorus also may not be palpable, and may not be felt at times; I shall return to these later to show that neither are necessarily present, but if they exist, they are

pathognomonic of certain cases of the affection. As to the peristalsis, we must be very careful also how we conclude as to its presence or absence, and this I shall also take up later for consideration. I will simply mention here a normal mild form of peristalsis seen in emaciated infants, which must not be confounded with the violent peristalsis I have described as present in some forms of this affection. Some of the most violent cases of vomiting with spasm or congenital stenosis of the pylorus have passed through my hands without the detection of the situation of the pylorus.

Some observers have endeavored to develop peristalsis by snapping the abdominal surface with the finger, or by palpating the stomach and causing the so-called "platsch" noise, or lapping sound, formed by fluid in the stomach. This I also regard as fruitless in considering the symptomatology of these cases.

Inasmuch as I intend to come back to the individual symptoms, I will pass on to a general consideration of other symptoms in these cases. There is no fever. The children, after having nursed, vomit, and, strange to say, will retain fluid which is given them immediately after vomiting. Some authors have been insistent on the physical signs revealed by percussion of the stomach, and have added dilatation of the stomach to the other physical signs in these cases. I must agree with Pfaundler and others that dilatation in the normal or abnormal infant is very difficult to establish, and it is questionable whether it can be proved. The stomach is so subject to variation in size that a percussion of the stomach will reveal very little as to its actual anatomical condition, so that a dependence on signs of dilatation of the stomach as proving the condition which we are discussing is of questionable utility.

I will take up the question as to whether in these cases there is a spasm or a distinct stricture of the pylorus or stenosis. I believe that there is a certain set of these cases, the subsequent history of which proves distinctly that there is at a certain period of the illness a spasm of the pylorus and stomach and at its pyloric end; that for certain reasons this spasm subsides and under favorable conditions the children cease to exhibit further symptoms of their condition, and recover. In other cases, in addition to this spasm of the pylorus there is added also a distinct anatomical condition in which the structure of the pylorus is abnormal; the muscular coats as well as the mucous membrane are thickened and thrown into folds, causing a narrowing of the orifice of the pylorus. This, with the spasm superadded, causes a distinct stricture at this point, which in some cases is extreme. In a great many cases, even this anatomical condition sometimes admits of improvement by relaxation of the stricture, cessation of the spastic condition at the pyloric end of the stomach and opening up of the lumen of the pylorus, and a continued improvement of the patient. In other cases this spasm of the pylorus may subside, but the lumen of the pylorus remains

narrow, and still the children may improve with correct diet. In other words, if the anatomical condition of narrowing of the pylorus is not complicated any longer with a spasm, which exaggerates this condition, a certain amount of food is allowed to pass through the narrow orifice into the intestine, is absorbed, and the children improve.

In this way only can I reconcile all the conflicting theories of this condition to be found in the literature. For example, Thompson, who published some of the first cases of this condition, insists that a muscular hypertrophy is superinduced by disordered coördination and contracture of the muscular coats of the stomach, including that of the pyloric end. This incoördinate contraction is initiated by the swallowing at birth of an irritating substance, such as liquor amnii. Its effects on the mucous membrane of the stomach itself are not at first apparent. After a few days or weeks it becomes apparent, and then the vomiting sets in. The overaction of the muscular coats of the stomach, including that of the pyloric end, are a direct cause of hypertrophy of the coats of the stomach. In other words, a form of functional hypertrophy due to overwork of the stomach develops.

Another theory which can only be reconciled by the peculiar set of cases seen by the observer, is that of Pfaundler, who insists that all of these cases are spasm cases, and the so-called new tissues or the hypertrophied pylorus, in some of the cases amounting to a distinct tumor, are the result of operative or postmortem contraction, and that such a contracture of the pylorus can be demonstrated at the autopsy table in most infants. I can only say that I feel that possibly Pfaundler had not seen at the time he ventured this theory some of the most aggravated cases of this condition, in which, during life, a hard unmistakable nodular pylorus can be felt through the abdominal wall. The question of postmortem contracture can scarcely enter into these cases, nor can operative contracture.

The third theory is that some of the subjects are born with a congenital anomaly at the pyloric end of the stomach, consisting of a form of newgrowth or hypertrophy of the muscular fibers that go to form the pyloric valve.

I will endeavor to show that all of these theories are in a sense possibly true of many of the cases published. I therefore will divide my subject into those cases in which we can only show from the clinical history and subsequent course of the case that there has been a distinct condition of spasm not only of the pyloric end of the stomach, but at the pyloric valve; and other cases, in which we can say from a study of the clinical symptoms that there is a congenital hypertrophy at the pyloric end of the stomach of the muscular fibers entering into the structure, in some cases so extreme as to indicate a narrowing of the lumen of the pylorus, a stenosis more or less marked, varying in different cases. Even such cases may make a

recovery or a partial recovery, and other cases, apparently exactly similar, will not, according to the opinion of some authors, allow of such recovery without operative interference.

The first set of cases which I wish to report and analyze are those in which there is an undoubted spasm of the pylorus and the pyloric valvular orifice, initiated, as it seems, by some error in feeding the child, by some toxic element which immediately after birth has irritated the stomach itself, causing a mild form of increased peristalsis; these become more disordered and violent, resulting eventually in the symptoms of spasm of the pylorus. It may be that in these cases there is a distinct contracture of the pyloric valve which may or may not be palpable. As a rule, it is not palpable through the abdominal wall.

In some of these cases peristalsis is not evident on the abdominal wall; on the contrary, in some of my cases it was absent. If there was peristalsis, it was of the *fruste* variety; that is, it was abortive. Only a very mild form is seen on the surface. In spite of this, the children vomit, and vomit not only after every nursing, but at times reject even more than is taken, on account of the peculiar condition of the pyloric valve, which does not allow the stomach to be completely evacuated in time for the subsequent nursings. In these cases also, there is, as in the so-called congenital hypertrophic stenosis, a residual amount of food in the stomach between nursings.

The outlook in these cases for the most part is very good. These are the cases which we see so frequently recorded in the literature as having made a recovery without operative procedure. It is surprising how many of them come under the notice of the physician who is especially interested in this line of work. The children in all of these cases are atrophic, or they have remained stationary in weight. Some even show a certain amount of nervous hypertension; they are easily frightened. When undressed and handled carelessly, they start to cry, as if frightened. Thus, as with the stomach, the whole nervous system seems to be in a condition of hyperacusis.

The first case of this kind is one which seems to me to be typical of this variety:

CASE I.—Female child, aged five weeks, one of two children, the other child having disease of the spinal vertebræ. The mother has never had any miscarriages, and is well apparently, but the father has a healed Pott's disease. The child is on the breast; it has had no previous illness. The present illness began nine days after birth when the patient began to vomit after each nursing. At first she vomited after every nursing, and then after every other nursing, varying from time to time. The vomit consisted not only at times of all the child had taken in, as the father practically illustrated to me, inasmuch as he collected all that the child had vomited, sometimes four ounces of the breast feeding, but it would vomit

after nursing more than it had taken in; and being a very intelligent man, he surmised that the infant had residual milk in the stomach, because when the child vomited the residual milk was curdled, and when it vomited at times when there was no residual milk there were no curds in the vomit.

The movements, scarcely deserving the name, were fluid, sometimes green and sometimes yellow. The child weighed five pounds thirteen ounces and was in poor atrophic condition. Examination of the other organs of the body, aside from the stomach, which I have mentioned, were negative.

No peristalsis could be seen on the surface of the abdomen, but the pylorus could be felt underneath the liver as a nodular mass, not hard, as in other cases I shall mention, but rather soft and cord-like. When the infant vomited, the abdominal muscles were rigid. The baby would nurse, after nursing would cry; there would be a contraction of the abdominal muscles, and the nursing was expelled. The vomited matter consisted of what the child had nursed, and when seen by me in my office contained a glairy mucus.

Examination of the mother's milk showed that it was very abundant, but at the fifth week it had a peculiar dirty appearance, so that evidently, from a gross physical examination, it was unsuitable for the baby.

This patient was sent to my hospital service and I had full opportunity to observe it. As soon as the child was taken away from the mother's breast it was put on a feeding at first of simple water, and was fed somatose by the rectum for twenty-four hours. The simple water contained a little citrate of sodium. After twenty-four hours the infant was placed on an ordinary percentage mixture of top milk, and each nursing was accompanied by a powder of citrate of sodium. The vomiting ceased as if by magic, but the child, in spite of variations of percentage of fat and proteids to within a limited period, refused to increase in weight on cows' milk mixture, and was put on a combination of the breast (wet nurse) and the bottle, when it increased slightly in weight. After it had been in the hospital for two weeks it was removed on account of an outbreak of measles in the ward and was sent home. It had vomited but twice in two weeks in the hospital. When at home, outside of my strict watch, on a wet nurse, it vomited only once a day, and did well. Having gained, the wet nurse was changed for economical reasons. The patient began to vomit again. The milk analysis showing 5 per cent. of fat. A change of wet-nurse again resulted in a cessation of vomiting. The infant is now thriving.

*Discussion.* This is a case in which we can say in all likelihood that the mother's milk was the direct cause of the child's vomiting, as also a subsequent wet nurse's milk. The mother states that after the eighth day the child was given in addition the bottle, and the vomiting followed. This administration of the extra bottle of milk, it appears

to me, with the irritating qualities possibly of the mother's milk, or the high fat percentage of the wet nurse's milk, have been responsible for the spasm of this stomach, which was of a purely toxic type. This case can scarcely be confounded with the so-called habitual vomiting of infants, which is quite frequent in practice. This child vomited to such an extent as absolutely not to retain anything on its stomach after the nursing, and at times only retained enough to ferment in the stomach and be evacuated at the next nursing. It had been under the care of a distinguished pediatricist, who had put it on dionin, without results.

Unfortunately we do not know the initial weight of this baby, but the mother states it was a plump baby when born. I feel that its future will be good, inasmuch as it has improved on the breast nursing.

CASE II.—The second case is a typical one of spasm of the pylorus, which came to my service at the Mt. Sinai Hospital. Female infant, aged seven months. The mother has tuberculosis and Bright's disease; otherwise the history is negative. One of her children died of meningitis at the age of eighteen months, the other is still living and well. This baby was born after an easy labor, but was never breast fed. It was fed on condensed milk and water for two weeks; it was in the Children's Hospital in Albany from August to October, three months before I saw it. At that time the child had diarrhoea, watery stools every day, sometimes green, sometimes mixed with mucus. The infant vomited almost every feeding. The vomiting consisted at that time of cheesy, sour smelling material. It never vomited blood, nor passed blood by the rectum; there was no cough. The child was admitted to the hospital, in fact, for this vomiting, although there are no data as to exactly when the vomiting began. When admitted to my service the child had general furunculosis; it was in miserable condition; it was restless, cried a great deal, did not sleep. For the past month the child has vomited daily; it vomited every feeding cheesy, sour-smelling material. The bowels were constipated, the child was losing in weight, and was extremely atrophic. When admitted to the service the child weighed seven pounds and nine ounces. It is not necessary to give the physical examination on admission as it does not bear on what has been noted.

In this case I studied the abdomen carefully after having first watched for peristalsis, but failed to get it in the empty condition of the stomach. When the feeding was given to the child, the stomach was studied. There was a very mild form of peristalsis present, and in spite of this no pylorus could be felt distinctly. The child was admitted January 5, and up to January 22, her weight ran down to six pounds and eleven ounces. She vomited practically everything that was given to her. Forced feeding was tried, and in this forced feeding at first citrate of sodium was added to

the milk. From the time of the forced feeding the spasmodic vomiting ceased, and was replaced by an occasional vomiting, until finally on January 26, when the citrate of sodium was given, the frequency of the vomiting dwindled to once a day, and after February 1 the infant practically did not vomit at all.

*Discussion.* This is a case which was closely watched. Out of eight feedings a day, at first the infant vomited from six to eight without any abdominal symptoms, and with a gradual diminution in weight. When the vomiting ceased the weight gradually increased until its discharge from the hospital, exactly one and one-half months after admission, weighing eight pounds and five ounces, an increase of two pounds over the lowest weight, that is, January 22, having been discharged February 16. This is a typical case of spasm of the pylorus without any symptoms of hypertrophy of the pyloric end of the stomach, and no marked peristalsis, in which forced feeding was resorted to for a few days, followed by the ordinary nursing, with an increase of weight and a tolerable cure of the condition. This case was under observation at times for the purpose of deciding whether operative interference would be necessary. The course of the case speaks for itself.

Another exquisite example of simple spasm of the pylorus without marked hypertrophy and possibly no great stenosis of the valve is the following case:

CASE III.—Male, aged four weeks, the only child. The mother has had no miscarriages, she and the child both being healthy. It was a forceps delivery; the child, weighing eight pounds at birth, was breast fed, had gained every day on the mother's breast until two weeks after birth, when vomiting began. The child vomited after every nursing for ten days previous to being seen by me. The mother allowed it to nurse as long as it pleased, she having plenty of milk, and her breasts at times caked. It vomited after every nursing sour, yellowish material of great quantity. The child had moderately large movements, which were greenish. When brought to me it weighed seven pounds and five ounces, was poorly nourished, atrophic in its condition. Physical examination was negative, and when observed it vomited during nursing, but when nursed again would retain its food. At the first examination there was no peristalsis and no pylorus could be felt. The vomited matter was large in amount; vomiting occurred almost immediately after nursing, and was projectile. The mother states that having vomited the baby will retain a second nursing quite well for at least half an hour. The mother's milk seems to be good in quality and color. I noticed, however, that the child had a traumatic stomatitis; its mouth had been washed and treated roughly.

In order to test whether the breast or the bottle was at fault, I placed the child on alternate breast and bottle feedings. I found that it vomited the breast more than the bottle, therefore I

stopped the breast entirely and placed it on the bottle. When seen a week subsequent to the first visit, there was a slight *fruste* peristalsis noticeable on the surface of the abdomen, but no pylorus could be felt. The vomiting continued after almost every feeding, the weight diminished to seven pounds four ounces, and still no peristalsis could be seen, but the pylorus could be felt under the liver in the neighborhood of the umbilicus like a thin cord-like structure. The child continued to vomit. After three weeks of observation it had diminished in weight to six pounds and fourteen ounces. The pylorus could then be felt as large as a bean underneath the liver half way between the umbilicus and the free border of the ribs. Whenever the child has a spasm of the stomach it cries as though in pain, and is only relieved when the vomiting occurs. In spite of loss in weight the infant looks well. The child is extremely nervous, hypersensitive, and when the spasm sets in the child starts, and then the vomiting occurs. After three and one-half weeks of vomiting the child was put on a wet nurse, and began to gain gradually. The wet nurse was changed, and it was then put on a very good breast, and the vomiting gradually ceased, taking place only once a day, and the child is doing well. It gained fully two pounds in one month of the new nursing.

*Discussion.* This is a case of clinical spasm of the pylorus which was closely watched for a month with the idea of possible surgical interference on account of steady loss of weight. The friends of the infant, including the mother, were intelligent people, understood the situation exactly, and coöperated with the observer. There was no question as to the vomiting; every particle of food taken into the stomach was rejected from the time of the observation until the infant was placed on a breast which was as nearly perfect as possible. The mother's milk evidently was responsible in this case for the initial vomiting, for as soon as the infant was relieved partly of the breast, this leading feature of the case subsided with the bottle feedings, although not completely so, and continued unabated with the breast. When the mother's breast was completely suspended improvement in the vomiting occurred, but the weight was rather stationary, if the child did not lose. With the ideal breast the vomiting ceased almost entirely, taking place only once in twenty-four hours.

Here are three cases of aggravated spasm of the pylorus, which I am assured would come under the classes, so frequently mentioned by Heubner, Pfaundler, and others, who insist that they can get well without operation. I feel also assured that possibly others, who have not had so many of these cases come under their observation, and who did not have the opportunity to observe them for the length of time that I had before an improvement set in, might have resorted to operation; not that I think operation would have harmed any of them; on the contrary, it might have resulted in



the infant's having been relieved of the spasm and improved more rapidly than with the preceding methods; but they illustrate perfectly how cases of simple spasm will not only improve and get well, but may at times be mistaken for another set of cases, which are still more aggravated in their symptomatology.

I will now take up the study of cases from my records of congenital spasm of pylorus, which at first showed symptoms fully as severe as those which have just been noted, but which improved rapidly under observation, or having passed from observation showed after many accidents and much experimentation with diverse forms of feeding, loss of weight to a most desperate degree, according to the statement of the attending physician. They then improved spontaneously on foods, which we as scientific men consider most unsuitable.

CASE IV.—R. O., male, native of the United States, aged six weeks, patient of Dr. S. The first child; mother never had any miscarriages; father and mother are in good health. At birth baby weighed seven pounds. When it came under observation the infant was fed partly on the breast and partly on the bottle. It had vomited since birth, and having vomited the breast, was taken off the breast and placed on an artificial feeding. The vomited matter was watery and acid; the baby had gained in spite of vomiting to a slight degree. At times it does not vomit at all; at others it vomits all that it has taken. The bowels have a good color, but the infant is constipated. The main food now is the breast, the mother having gone back to it after several vain attempts with the bottle. The weight of the infant is seven pounds and seven ounces; it is in tolerably good condition, although atrophic. The physical examination is negative, and a study of the abdomen gives no peristalsis. Diagnosis: spasm of the pylorus.

The infant having been taken off the breast and placed on a substitute feeding, did not improve, and disappeared from observation, having tried no less than three different kinds of foods within two months. It vomited everything, the vomiting having increased since the first visit, a period of two months; spits up, if it does not vomit. Vomits a little at each feeding, and vomits very severely twice a day all that it takes in. After another week of attempted feeding with foods which I shall not mention here, the vomiting continued about after each feeding. After an interval of about two weeks I saw the child again, and the vomiting continued. The increase in weight in two weeks was one-quarter of a pound. The child then disappeared from observation. The parents were very much opposed to placing the child on a wet nurse, and seemed rather determined to have the child die rather than resort to that method of feeding, having peculiar views on the subject. The child continued for two months, and lost in weight from the time I had first seen it to such an extent that the attending physician had made up

his mind that operative procedure would be necessary. He then placed it on a patent food, and strange to say, from the moment the trial of a new food was made, which was simply one of probably dozens which had been tried, the child stopped vomiting and began to gain in weight. Lately I had occasion to see the child, and I have never seen a handsomer baby than the one brought up on what I have always considered, and still consider, a very unsatisfactory food. The baby was eight months old when it was recently presented to me and weighed eighteen and one-quarter pounds, had a rosy hue, was firm in its muscles, and seemed to be perfectly happy. This case never presented any peristalsis, nor could I at any time feel the pylorus.

CASE V.—Edith O., aged three months, the only child, one child having died after circumcision; parental history negative; four weeks on the breast, and then was placed on a top milk mixture. It vomits after every feeding either one-half or all that it has taken in; the movements are constipated, small, dark, and undigested. The vomiting began four weeks after birth, when the child was taken from the breast and placed on the artificial feeding. The initial weight at three months was eight pounds and ten ounces. Its general condition was negative. I found no peristalsis, nor could I feel the pylorus. The child was put on an artificial food mixture and did well; although the vomiting continued to a mild degree, it continued to gain on the new food, but very slowly. It remained under observation until it was eight months old, when it weighed eighteen pounds. When fourteen months old it was brought again for observation, and weighed twenty-two pounds and eight ounces, and was in excellent condition.

CASE VI.—Harold G., aged six weeks, the first child; parental history negative; was brought up from birth on the bottle; has vomited since two weeks after birth after each feeding, not very much, but "considerable," as the mother puts it. It has vomited all that it has taken, but it is difficult to determine how much. The weight is eight pounds and five ounces, its general condition is good; the slightly contracted pylorus could be felt; there is no peristalsis. A diagnosis of spasm of the pylorus was made. Given a new food, the infant continued to vomit, but gained slowly, and during the entire period of observation the child continued to vomit, but gained steadily, so that after being under observation for six months it had gained nine pounds, and after this continued to thrive. At nine months of age it weighed seventeen and one-half pounds.

CASE VII.—Male infant, aged two months, patient of Dr. O. One of two living children; parental history negative. The child was given the breast at first for three weeks, and is now taking a Walker-Gordon percentage mixture. The baby has vomited since birth, sometimes a half or three-quarters of an hour after feeding

it vomits all of the feeding: the milk is curdled, but in spite of this it has gained since birth three pounds. The movements are green, and it has several passages a day. The child suffers from considerable flatus. The weight is ten pounds and two ounces; the general condition is good; physical examination negative, except there is distinct peristalsis visible on the abdomen after feeding, and the contracted pylorus can be distinctly felt. This baby, after considerable coaxing and the addition of sodium citrate to the food, so improved that the vomiting ceased gradually; the child continued to gain, and remained a healthy child free from vomiting.

CASE VIII.—Female infant, aged four months, one of two children; parental history negative. Was given the breast a few weeks, and then was put on the breast and bottle. It has vomited since birth nearly the whole of every feeding. Gets the breast twice a day, and for the remainder of the feedings a top milk mixture. It vomits after every feeding nearly all it takes in. The bowels are fairly good, one or two movements a day, has no colic; has only gained four ounces in two weeks. The initial weight at birth is not given, but when seen it weighed eleven pounds and ten ounces, and, although atrophic, was in good general condition. Physical examination negative. There is no pylorus to be felt, although there was an indefinite soft band underneath the liver. A diagnosis of spasm of the pylorus was made. This child was under observation for three months, during all of which time it vomited, but it gained slowly, and at the end of the three months it weighed fifteen pounds (seven months old). It still vomited, but only about a tablespoonful of each feeding. It then passed from observation presumably doing well.

CASE IX.—Female infant, aged six weeks, patient of Dr. H.; the only child; parental history negative; weight at birth not given; fed on the breast two weeks, and then was put on a mixture of patent food and milk, although it was given condensed milk and later percentage Walker-Gordon mixture. The baby vomited, though not at first on the breast. Toward the end of two weeks of life it began to vomit at every feeding; had many movements of a watery character, some colic at times. On the percentage mixture it was constipated, and then, through some milk poisoning it had many movements. At the first visit it vomited every bottle and two or three times a day almost all of the feeding. On close observation, slight peristalsis after feeding, and the child seems to suffer after taking the food. There is no palpable pylorus. A diagnosis of spasm of the pylorus was made. This infant came under observation with a weight of six and one-quarter pounds. In a month it gained one and one-half pounds; under careful feeding the vomiting ceased, although at first it continued; the movements were regular, and at times it would have a diarrhoea. It remained one month under observation. The

subsequent history is that the child did very well and is continuing to improve.

CASE X.—This case is one which I saw a number of years ago, and for that reason the history is only partial. It was an only child, female, aged seven months, fed on the breast for a few weeks and then had sterilized milk, peptonized milk, and finally was put on sterilized milk, two-thirds to one-third water. Is very much constipated, rejects a certain amount of several bottles, and vomits a great deal twice a day. The diagnosis at that time was pyloric spasm. Under an appropriate feeding the child continued to improve, but vomited under all feedings, although not so much as it did at first. It was under observation fully a year. At the end of that time it weighed twenty-five pounds, and was a well-nourished child.

It will be seen from what I have just recorded that there are varying degrees of spasm of the pylorus, some of them exceedingly severe, so as to place one in doubt as to the proper therapeutic procedure, and cause great anxiety as to whether any kind of feeding will agree with the child. To show to what extent the process of waiting may be resorted to in these cases, I may, in closing the chapter on the spasm of the pylorus, record a case which was celebrated in its day.

CASE XI.—This child at the age of seven months weighed eleven pounds; an only child; being at first on the mother's breast, began vomiting shortly after birth. The physician in charge placed the infant on a wet nurse. The vomiting became more severe, the child restless at times, to such an extent as to rob it of its sleep. It vomited everything that was given to it. In spite of this the infant was carried along to the seventh month, and almost every physician in New York with any knowledge in feeding had seen the child, and one eminent pediatricist had advised operation as a last resort. When I first saw this child it was exceedingly atrophic; it vomited every bottle that was given it, and almost every kind of feeding known to science and empiricism had been tried. It not only failed to gain, but failed to retain its food.

I was called in simply because the parents absolutely refused to entertain an operation until they had tried one more resort. Physical examination was negative; no pylorus felt; there was no peristalsis. As in many of these infants the abdomen was rigid, and when the infant nursed the bottle, immediately afterward, there was great restlessness, evidences of pain, and the food was rejected. In spite of this the infant held its own at eleven pounds, at seven months of age. It was constipated, the movements were very small. I made a diagnosis of spasm of the pylorus and temporized for a week on an artificial food, which was also rejected. I then suggested a wet nurse, and was informed by every one connected with the case that I had not been called in for that purpose, but

rather for the purpose of trying to give the child an artificial food. I enlisted the attending physician's aid, and promised to obtain a wet nurse for him if he would place the infant at the breast. He promised to do this. From the moment the infant was placed at the breast it commenced to gain in weight, the vomiting gradually ceased and disappeared. The change was simply miraculous. At the age of fourteen months the baby weighed twenty-three and one-half pounds, and was a perfect infant to look at.

This is a case which I think was spasm of the pylorus, in which the diagnosis of congenital pyloric stenosis was made, and in which operation had been advised and held out to the parents as a last resort by physicians whose skill in diagnosis and in treatment of infants is undoubted. But this infant acted like most infants with this affection, it strangely began to improve on the proper feeding, and doubled its weight after seven months.

I hope I have recorded enough cases to show from my experience there is such a thing as *spasm* of the pylorus pure and simple, resulting in constant vomiting and stationary or diminished weight, and a certain amount of suffering to the infant, some infants threatening to pass out of existence unless aided by some heroic measure, such as operation, but all of them improving under the steady prodding of scientific and intelligent feeding. As I have before stated, some of these cases might have been operated upon with a certain amount of justice, and yet I could not find reason for such interference, at least from personal observation at certain stages of the illness. I was fortunate to hold the patients to the last minute until improvement set in, and I have been able thus to demonstrate the practicability of waiting and trying in these cases.

I shall now pass on to the consideration of a condition which I think is an exaggerated state of what has been just pictured, in which not only spasm of the pyloric orifice exists, as well as a spasmodic contraction of the pyloric end of the stomach and the cardiac portion, but in which there is a distinct hypertrophy of the pyloric valve and its structures, a narrowing of the lumen of the pylorus to such an extent as to constitute a distinct growth of new tissues, which can be demonstrated by palpation of the abdomen, and certain other symptoms. In these cases there is a distinct and disordered contraction of the stomach, which is visible on the surface of the abdomen. The peristalsis, so-called, of the stomach is so marked that in the severe cases the stomach seems to erect itself, that is, the cardiac end upon the pyloric end, as if the cardiac end of the stomach was making a supreme effort to drive the food through the contracted pylorus. In these cases the pylorus can be felt distinctly as a hard nodular mass underneath the liver, sometimes midway between the umbilicus and the free border of the liver.

The theory in these cases is familiar from the literature, and it

is, that we either have, according to Thompson, an hypertrophy acquired through the disordered contraction of the stomach, or a congenital condition originating in the uterus and manifesting itself after birth. Under this latter theory we would have a sort of new growth replacing the normal structures at the pylorus.

The third theory, that of Pfaundler, is that the pylorus, which has been found on operation to be thickened and hypertrophied, is simply as found in other normal stomachs postmortem. I have taken up this question in the early part of the paper, and will not repeat any more than to say that some of the cases, which I have recorded as spasm of the pylorus, would fit the Pfaundler theory more completely than the case which I now record.

*CASE XII.—Congenital Hypertrophic Stenosis of the Pylorus.*

The first case of this kind which I shall record was one which came to operation. The patient was a male child, five weeks old, the first child; parental history negative; the weight at birth not known. The mother gave the breast for two weeks. She seemed to have a normal quality of milk. The baby had vomited from birth, vomited after every nursing; the movements were normal, and the vomiting began the first week after birth. It weighed, when first seen, eight and one-quarter pounds. Its general condition was good, physical examination of the organs negative. At first there was no peristalsis, no pylorus was felt. The mother's milk was not so very satisfactory, in that it was not abundant, and was whitish in color. The provisional diagnosis of pyloric stenosis was made. The patient, under observation, was seen to vomit not only everything it had nursed, but seemed to vomit more than it had nursed at a single feeding. In other words, there was residual milk in the stomach. The vomiting occurred about fifteen minutes after feeding and was slightly curdled. The child was taken off the breast and placed on modified milk, and did not improve. It was then placed on two wet nurses, the wet nurse having been changed, with slight improvement only. The bowels were constipated, the movements small, yellowish, and tape-like. It had lost in one month one and one-quarter pounds, having been nine pounds at birth.

When admitted to the hospital, to which it was sent for further observation, the abdomen was tympanitic, and there was visible peristalsis on the abdomen, from left to right, stopping suddenly at the pyloric end of the stomach. The pylorus could be felt two inches below the tip of the ninth costal cartilage, as a round movable mass, the size of a small chestnut. After observation for some days it was found that the peristalsis increased. A wet nurse was procured, but the vomiting continued, the weight having diminished, so that just before operation, which took place a few days after admission, the child had lost three-quarters of a pound, being six and one-quarter pounds. The peristalsis became more disordered

and visible. The child cried after every ingestion of food, just before it vomited. After nursing from the wet nurse, the stomach would erect itself fully three-quarters of an inch upon the surface of the abdomen, as if attempting to drive the food through the pylorus, the child being uneasy all the while, and then vomiting of almost all that the infant had ingested would occur. In view of the fact that the infant was losing ground and looked extremely prostrated, Dr. Lillienthal was asked to see it, and agreed to perform a posterior gastro-enterostomy. After operation, the child continued to vomit on the wet nurse, and was placed on artificial food. The first twenty-four hours after operation nothing was given but water, the child being exceedingly low. He then seemed to come to the surface. He vomited the food and some greenish matter, and finally, when placed on the artificial food, which was retained much better, improved to a remarkable degree and recovered.

I may say, without going into the surgical details of the case, that Dr. Lillienthal, wishing to finish the operation very rapidly, could only partially investigate the condition of affairs in the abdomen. He confirmed the presence of the pylorus, hypertrophied and hard, and fixed to the posterior wall of the abdominal cavity. It is not necessary to go further into the case than to say that after the operation the infant vomited several times a day small quantities of greenish material, feeding having been begun twenty-four hours after operation. After five days of unsuccessful feeding on the breast, the infant not increasing in weight, artificial feeding was again attempted, and after a few accidents, the pulse at one time, having become rapid and feeble, and Dr. Lillienthal having thought the child would be lost, it began to rally, made a very good recovery, and on its discharge from the hospital, it weighed seven pounds and ten ounces, a gain of one pound and six ounces over the lowest weight before operation. The infant then continued to improve under observation at home, and weighed twenty-two and one-half pounds at the age of fifteen months. I have since seen the child at intervals, and it remains perfectly well and has absolutely no gastro-intestinal symptoms referable to the pylorus or operation.

*Discussion.* This is a case of undoubted congenital hypertrophic stenosis of the pylorus combined with spasm of the pyloric and cardiac end of the stomach, with vomiting to such an extent as to endanger the life of the patient. With the mature judgment of the surgeon and physician the infant was operated upon successfully. It is, of course, impossible to say, in view of the low condition of the child after operation, whether continued attempts at feeding might not have succeeded in this case. It is enough to record, however, that our feeling at the time was that should we wait much longer, we would lose the child, and this, to our conscience, seemed sufficient justification for the operation. The fact that the

child improved after the operation is, of course, no proof that the operation was absolutely indicated; still, it was the only thing that we could possibly think of, if we intended to save the life of the child at the time.

**CASE XIII.—*Congenital Hypertrophic Stenosis of the Pylorus; Operation; Death; Autopsy.***

L.S., male infant, aged seven weeks; family history negative. At birth, infant was normal; normal delivery, with no history of previous disease. Nursed at the breast for five weeks, then the breast feeding was omitted and re-commenced. The break in the breast feeding was made by that of artificial feeding, which was continued after the breast was commenced again. Three weeks before admission to the hospital the infant began to vomit; the movements were green curdled; there was a slight cough. It improved for a few days, then became worse and vomited and was constipated, and when the bowels did move, they were greenish. Both ears had been discharging for the six days before admission to the hospital. There was some fever, great loss of weight; the principal complaints were vomiting, constipation, and loss of weight. The physical examination was negative, with the exception that there was a discharge from both ears, the mastoid region was negative; the mouth presented marked stomatitis, tongue coated, the inguinal glands slightly enlarged. The abdomen was lax, tympanitic, nothing palpable, no tenderness, but there was visible gastric peristalsis.

The day after admission we have the following note: Patient vomits within a few minutes after each feeding, peristalsis takes place a few times, then the entire feeding is vomited. No tumor can be felt. There is a sense of resistance in the right hypochondrium in the region of the pylorus. The patient retains nothing on the stomach. The next day a regular feeding was given and the infant studied. Peristalsis was visible before feeding, and became much more marked after feeding. After several waves of peristalsis, the feeding was expelled. The expelled food was at times mingled with a yellow greenish fluid. Immediately after feeding the pylorus could be distinctly felt beneath the liver in the right hypochondrium, between the free border of the ribs and the umbilicus, as a round hard substance.

The next day a test meal was given, and later recovered. The test meal consisted of three-quarters of an ounce of food, and at the end of one-half hour one-half ounce was recovered, a thin whitish fluid showing small milk curds, and moderate amount of mucus; reaction was acid. There was free hydrochloric acid; total acid was 38, combined acids 22; no lactic acid, no blood; microscopical examination negative. The stomach washings were positive to rennet; pepsin positive, but weak on account of dilution, negative as to free hydrochloric; combined acids 6 c.c. per hundred; peptone was present. Two days after this another report of the



gastric contents showed acids 24 c.c. per hundred; free acid absent, positive to rennet, positive to pepsin, peptones present. The vomiting continued, the child losing in weight.

Dr. Lillienthal saw the patient in consultation, and agreed to the performance of an operation for the relief of the pyloric stenosis. The stomach at the operation was found distended and somewhat prolapsed. At the pylorus a smooth mass the size of a walnut was felt, very much like an intussusception; the transverse colon was drawn up over the stomach. A posterior gastro-enterostomy was made, the surgical details of which I will not go into. The temperature before the operation was  $103.6^{\circ}$ , probably on account of the otitis; unfortunately, after the operation the temperature rose; the region of the left mastoid became swollen, so that relief of this condition seemed imperative. An incision was made, a conservative opening of the antrum was effected; it was filled with pus. The wound was packed in gauze, but the child died twenty-four hours after the mastoid was opened.

*Postmortem.* Specimen obtained showed the hypertrophic condition of the pylorus and the narrowing of the lumen of the valve. The stomach, however, was not dilated; on the contrary, it seemed to be smaller than normal. The posterior gastro-enterostomy showed no leakage. The infant probably died as a result of the shock of the operation.

*Discussion.* In this case the unfortunate ear complication, necessitating even a conservative interference, rather militated against the recovery of the child. The good judgment of the surgeon demanded the primary operation, and it seems as though possibly, had the child had a little more resistance, it would have recovered from its malady. (It is hard to tell, even in this case, whether temporizing would not have resulted in an ultimately better condition of the child, but the child certainly did badly before the operation, and there seemed to be no other course open to our judgment.)

I wish to record a case which shows an interesting phase of this subject, that is, that children exhausted by gastro-intestinal intoxication, starvation, and pain may die suddenly before aid, either through feeding or surgery, can be instituted; that is, while waiting for an improvement or for a decision of therapy, the patient suddenly dies.

CASE XIV.—E. S., female infant, aged seven weeks. The only child; no miscarriages; parental history negative; was nursed for three weeks on the breast, and then the breast was combined with a bottle feeding containing top milk. The present illness began almost immediately after birth; the infant vomited every feeding. Among things which had been tried, the infant was placed on the breast of a wet nurse. There were no movements of any moment, evident constipation. When seen the initial weight could not be

obtained. At seven weeks the infant weighed six pounds; its general condition was very poor, and it was emaciated. To one side of the median line, beneath the liver, and above the umbilicus the contracted pylorus could be distinctly felt. The child vomited at every feeding. A diagnosis was made of congenital hypertrophic stenosis of the pylorus. A test nursing was vomited in the office at the first visit. The infant was temporarily placed on what was considered a better food and a wet nurse advised. The father reported the next day that the child had died in bed.

*Discussion.* This infant when brought under observation was no worse than many infants I see with similar affections. It was very ill, but there was nothing to warn one, except the extreme weakness of the child, of the sudden demise, and when compared with the following case will be of interest to those who are anxious to know the latest period at which interference of a surgical nature is permissible.

CASE XV.—R. B., male infant, aged eight weeks. First child; seen in consultation with Dr. W. Family history negative. At birth it weighed six pounds and fourteen ounces. It was fed at first with modified percentage mixture, and then was placed on a wet nurse. It was perfectly well and nursed well, and gained in weight until three weeks after birth, when it began to vomit. Previous to this it had always retained its feeding. The vomiting continued. Sometimes three or four feedings a day were vomited, and the others were partially vomited. The infant lost in weight, and after two weeks of experimentation with infant foods and stomach washings the infant was placed on the breast of a wet nurse. It then began to vomit more than before, and the loss of weight was more palpable. When seen first it was in the eighth week of infancy; weighed five pounds and nine ounces, having lost one pound five ounces of its initial weight. Its general condition was exceedingly poor and marantic; the skin hung in folds on the body. The physical examination was negative, but the infant had a double inguinal hernia. It had a mild form of peristalsis, and after a trial nursing there was no vomiting, and I proposed that a new wet nurse be tried. On the new wet nurse the condition was as follows:

There were two, sometimes three, vomitings in twenty-four hours, in which all the food taken into the stomach was rejected, and then the infant would vomit varying quantities of the other nursings. Peristalsis on the abdomen was very apparent, and at times tumultuous, even between the nursings. A small nodular mass, the size of a white bean, could be felt underneath the liver, half way between the free border of the ribs and the umbilicus. The infant seemed to be uneasy, and cried during peristalsis, but nursed with great eagerness. The infant was under observation for five days, and during that time the movements were semifluid, yellow, and to

my mind not sufficient in quantity to show that much food had passed through the pylorus, but only a fractional amount of what it had nursed. At the consultation the advisability of operation was freely discussed, but, on account of the extremely weak condition of the infant, interference was postponed for at least three days, for further observation. The child was given dionin,  $\frac{1}{100}$  of a grain, three or four times a day.

The subsequent history of the case is exceedingly interesting. The vomiting continued as well as the peristalsis, but the infant seemed to hold its own. It had gained three ounces under observation, and had fallen back three ounces in the week in which it was observed, leaving its weight five pounds and nine ounces. The infant seemed comfortable, however, and after a few days of additional observation the vomiting became less frequent, and the infant slowly gained. The vomiting finally ceased, the weight increased, but the peristalsis continued for some time, being visible through the very thin abdominal walls. After five weeks the infant had gained ten ounces.

*Discussion.* This case, after conscientious observation, seemed to be one in which operation was certainly indicated. The operation was only postponed because, to the surgeon, the infant appeared too weak, and its chance of recovery from the operation too small, and still this infant improved without operation, and continues to improve today. The increase in weight is not such as would encourage us to predict the future of the infant; at the same time, no one can convince himself, in face even of an increase in weight of three-quarters of a pound a month, that any surgical interference was warranted. This infant was certainly as weak as the previous infant, which died suddenly, too weak, in fact, to tempt the surgeon to operate, and yet improved in spite of the severity of the symptoms and the gloomy outlook.

*DIAGNOSIS.* In the diagnosis of these cases we should try as much as possible, from a clinical standpoint, to distinguish between the two conditions which I have discussed—those in which there is a spasm of the pylorus without any palpable hypertrophy of the tissues entering into the formation of the valve or the pyloric end of the stomach, and those in which the clinical distinctive features, which have been described, warrant the diagnosis of congenital hypertrophy of the pylorus with spasm of the cardiac and pyloric portions of the stomach, causing a narrowing to a greater or less degree of the valve.

First, in simple spasm there is the persistent and full vomiting; the retentive vomiting present in the cases of congenital hypertrophic stenosis; there is also the steady emaciation and the constipation. There may be no peristalsis, and the pylorus, if palpable at all, is only felt as a small contracted nodule, not as hard or large as in the cases of hypertrophic stenosis. There are

also, once or twice daily, stools which contain a certain amount of milk feces.

In hypertrophic stenosis all the symptoms mentioned are present to an aggravated extent, but in addition there is marked and disordered peristalsis visible on the abdominal surface. This peristalsis is generally in one direction, toward the pylorus, which in a great number of cases is distinctly papable. The constipation is also more inordinate, and the stools show little or no milk feces, only bile-stained mucus.

X I have endeavored to distinguish these two sets of cases, of spasm and of congenital hypertrophy of the pylorus, with broad, distinguishing characteristics, and not by indefinite academic lines. The clinical study of the cases will place them in either class.

Congenital conditions, such as real growths of the pylorus or atresia of the pylorus, are exceedingly rare, and can scarcely be brought into consideration in connection with conditions which are considered in this paper. The symptoms in congenital atresia and growths which completely obstruct the pylorus must come on immediately after birth, and are rapidly fatal, unlike the conditions in which the symptoms appear some time after birth. Congenital stenosis of the jejunum or duodenum may be confounded with that of stenosis of the pylorus, if the congenital atresia of the gut is situated high and near the pylorus. There may then be a series of symptoms on the part of the stomach indistinguishable from those of pyloric obstruction. Pure pyloric spasm, I feel, may well occur and does occur with very slight hypertrophy of the pylorus, giving rise to only a limited form of stenosis. Ibrahim doubts the existence of pure pyloric spasm, but I have tried to show that it does occur, and this also in quite a percentage of cases; more especially is this so in those cases of persistent vomiting in which there is sudden or gradual cessation of symptoms upon the inauguration of correct diet and feeding. I think, in considering the question as to whether a spasm or severe form of stenosis is present, one of the most useful clinical guides is the amount and quantity of the stools. If in a given case the stools consist mostly of bile-stained mucus and very little fecal matter, in spite of the ingestion of an ideal food, such as breast milk, we are driven to the conclusion of the presence not only of spasm of the pylorus, but also of narrowing and stenosis of high degree. If, in spite of vomiting at every feeding, peristalsis and even a palpably contracted gut in the region of the pylorus, there is one or two stools daily containing some milk feces, we must feel, as in certain of my cases which at times appeared hopeless, that the stenosis at the pylorus is not of high degree, and that the spasm relaxes at times and allows of a certain amount of food to pass and nourish the patient. It is in most of these cases that we can feel that the ultimate out-

come will be favorable, no matter how exasperating present symptoms appear to be.

**PROGNOSIS.** The ultimate fate of these cases is extremely interesting in view of the recent contention from some quarters that as soon as the diagnosis of hypertrophic congenital stenosis is made the surgeon must interfere in behalf of the infant. I have tried to show that a large number of cases are really spasm cases, and will eventually recover on internal therapy. Persistent trial of feeding, the most diverse, will eventually result in overcoming the condition.

In one of my cases, a food was finally successful which is known to be an entirely unsuitable one in feeding infants over long periods of time. Why does the spasm relax in these cases, or cease after having continued for months? I have only one theory to offer, and it is that after a time, as in other nervous affections, there is a nerve exhaustion, the system becomes immune to the intoxication, or the intoxicating substance is excreted more rapidly and its action on the mucous membrane and nerve filaments of the stomach becomes nil and inefficient, the nerve tension exhausts itself, the spasm relaxes, and then any food that is digestible and assimilable will be effective in bridging the crisis. Thus, a food that at first would have been unsuccessful will in the relaxed period succeed.

As to the ultimate prognosis of true hypertrophic stenosis, my feeling is that there can be no general statement that will fit all cases. Most cases, I am certain, may be bridged over their crises by persistent attempts at feeding. It would also appear, from at least one of the cases here recorded, that ultimate recovery, even in the face of extreme exhaustion, is not impossible without operation, and we cannot but feel that most cases will escape the surgeon and only the rare cases reach the operative phase. This is only one fact which needs discussion in certain cases in which operation was refused and in which vomiting and other symptoms have subsided and the patients made an apparent recovery. This fact has not been mentioned in any of the many monographs on this subject.

Cessation of vomiting and all distressing symptoms does not constitute a complete recovery; the infant must also increase in weight and develop in a normal manner. I have lately met an illustrative case which in early infancy presented all the symptoms of hypertrophic stenosis of the pylorus and in which the symptoms persisted until the sixth month of life. They then ceased. The infant not only did not gain normally in weight, but developed the most aggravated symptoms of malnutrition. A well-known pediatricist had advised operation; but on reflection this advice was rejected by the parents. Today the child is a rachitic dwarf, aged two years, weighing twenty-one and three-quarters pounds, with a very marked lordosis of the lumbar spine, and a height of only 61 cm. This condition, fortunately extremely rare, is a direct result of lack of nutrition dependent on the pyloric condition in

infancy. Today this child is able to partake of all kinds of food, has no sign referable to the pylorus, but is physically a human caricature. This is an exceptional ending, for most of the cases I have described as recovering have done well, and in the end approached the normal in weight and general appearances. There is another contingency which is striking in those cases which have recovered without operation. That is, in after childhood there remains an indication of pyloric contracture and spasm. A case I saw recently was that of a male child of very good development, who during infancy showed symptoms of spasm referable to the pylorus. The child was brought to me because, whenever solid food was partaken by him he would complain of gastric pain and then vomit the solid particles. Such a case might fit in the class of cases occurring in later life and described by Landerer.

**TREATMENT.** I shall consider for the sake of conciseness: (a) Feeding; (b) mechanical means of therapy; (c) drugs; and (d) operative means.

*Feeding.* In a given case of hypertrophic stenosis or of congenital spasm the feeding is undoubtedly by far the most important element in the treatment. Breast feeding is the ideal method of feeding these cases, but not every breast will be found adapted to the infant. The breast is given at long intervals and short nursings. Many infants who have not improved on a given breast, or to whom a breast is not available, will be tided over their illness by some of the many and diverse forms of substitutes for the breast at command of the physician. I do not think any artificial food is ideal, and no one is a panacea in this condition. Some insist that the food contain a minimal fat, and I have shown that many cases have recovered on food which all pediatricists agree is the most unsuitable in the long run under ordinary conditions. In other words, though this condition seems in a certain proportion of cases to have been inaugurated by some error in diet, there is no royal road to the feeding. In artificial as in breast feeding the method must presuppose small amounts at each feeding, at long or short intervals, as the case may be.

*Mechanical means of therapy* include the application of warm cataplasms of flax seed and hops, or dry warmth, stomach washing, and enteroclysis. Stomach washing, I feel, is a useless and in some cases, when the infant is in a weakened condition, an exhausting procedure. Some of the cases which are detailed in this paper had been treated early by stomach washing without avail, and others with a distinct exacerbation of symptoms. All of the cases I have noted have eventually recovered without it. Enemas are useful in the form of enteroclysis of small amounts of normal saline solution to maintain nutrition. They are given several times daily.

*Drugs.* Heubner advises opiates, others derivatives of opium, in very small amounts to quiet the spasm of the pylorus and adjacent

stomach wall. Heubner uses the tincture. In most of my cases no opiate was resorted to, and in only one was it given, and then only after improvement was well inaugurated and only in exceedingly small doses and at desultory intervals. I have found but temporary benefit from the administration of citrate of sodium, or sodium and pancreatin.

*Operative Therapy.* An operation such as is proposed for the relief of congenital hypertrophic stenosis of the pylorus presupposes great technical skill on the part of the surgeon, and great dexterity and rapidity. One surgeon may complete the operation of posterior gastro-enterostomy in fifteen minutes, another in forty-five minutes. The difference to the patient can better be imagined than described. Again, a mortality of 50 per cent. (Ibrahim) to 75 per cent. is certainly not an encouraging prospect for the physician to hold up to the anxious parents. We are asked to hand these cases to the surgeon before it is too late. Who will say, and how are we to decide the proper moment when all further attempts to save the patient will be hopeless. I confess, with all my experience with these conditions, I still feel that my chances with nature are as good, if not in some cases better, than with the operative measure.

There is another point which I especially wish to consider, and that is, that the cutting out of a portion of the gut, which results when posterior gastro-enterostomy is performed, is not without harmful influence. The infant who has been recorded in this paper as having been successfully operated upon, did very well up to the eighteenth month of life, and presented no symptoms referable to the operation. He has, however, lately shown an anemia which does not yield to treatment, a rachitis of very marked degree, and late in its development. He presents also respiratory apnoea and, what is most peculiar and especially interesting to the surgeons, symptoms which point to a narrowing of the artificial opening in the stomach. The child is beginning to vomit after the ingestion of solid food; even small pieces of cracker cannot be partaken of without danger of a vomiting spell following immediately or soon after the meal. Meat the little fellow refuses to take, inasmuch as he feels that he will have to reject it. About two years after the operation symptoms of possible stenosis of the artificial opening in the stomach are beginning to develop.

**THE THERAPEUTICS OF SELF-REPAIR.<sup>1</sup>****BY S. J. MELTZER, M.D., LL.D.,****HEAD OF THE DEPARTMENT OF PHYSIOLOGY AND PHARMACOLOGY OF THE ROCKEFELLER  
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Numerous facts in biology justify the conception that the living organism represents a mechanism, and is in very many respects comparable to a complex human-made machine. Such a view proved also to be practical and very fruitful in the investigations of biology and medicine, since it encouraged the extensive study of the details of the living mechanism by the well-established methods of physics and chemistry. For therapeutics, however, this view seems to contain an inimical and discordant element. Therapeutics means the principles and methods employed in the repair of the disordered living organism. Now, the efficient repair of the mechanism of a human-made machine justly presupposes a familiarity with its normal structures and construction, and also a complete understanding of the nature of the disorder. But what is the status of our understanding of the living machinery and its disorders? Well may we point with pride to the great strides we have recently made in this understanding. But what is the actual extent of our knowledge? It may be freely admitted that it is very small, and is only an infinitesimal fraction of that knowledge which would enable us to comprehend the living machine as a competent engineer understands the human-made machine. And what is more, in the human machine physical and chemical forces may be, and probably are, active, but of their nature the present sciences of physics and chemistry have not even an inkling. Shall we follow the requirements of the human-made machine and wait with our therapeutics until we know all that?

While, thus, no man would be permitted to meddle with some serious disorders of a human-made machine with only a fraction of knowledge of its construction, we find that with the disorders of the mechanism of life for thousands of years millions of men meddled with their repair with a knowledge infinitesimally small indeed, even when compared only with the present-day understanding of the processes of life and their disorders. The contrast is still more striking when we consider the difference in the results. No man can be in doubt as to the outcome of an ignorant meddling with a human-made machine; it would lead, in the great majority of instances, to its complete destruction. But with the human organism, no such disastrous results followed the innumerable ignorant meddlings with its disorders; at least, such evil results were not

<sup>1</sup> Read at the meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1908.



readily recognizable: otherwise medicine would long ago have been wiped out of existence.

The truth of the matter is, that with regard to therapeutics the living animal body ought not and cannot be compared with an artificial machine. With respect to repair, there is a fundamental difference between a human-made machine and a living organism. The disorders of a machine can be repaired only by human hands. No machine has yet been invented which can automatically repair its own disorders. The living organism, however, is well provided with such automatic arrangements for self-repair. This fact has a far-reaching theoretical and practical importance. The fact itself, namely, that the living organism can master, unaided, its own disorders, was recognized very early in the history of medicine. Its true significance, however, was never fully grasped. In olden times, as well as in our modern era, it was utilized only as a weapon to discredit the claims of artificial therapeutics. It was pointed out over and over again that patients get well without any treatment, and if they get well under treatment, it might be that they do so, not because of it, but perhaps even in spite of it. The scientific labors of recent years, however, demonstrated clearly that the knowledge of the body's great ability for self-repair, far from being an inimical element to therapeutics, can be utilized as an element of great strength in support of the human efforts to cure or to hasten the cure of its ills. In the brief time at my disposal I shall devote my attention chiefly to a discussion of the aspect of therapeutics from the point of view of our knowledge of self-repair. I wish, however, to preface my remarks with the following brief statements, which, although self-evident, are nevertheless not superfluous.

Science and practice of medicine exist for the benefit of the sick, and therapeutics is the most important part of medicine. To be content with the mastery of pathological anatomy and diagnosis, and to have a contempt for treatment, is a moral and intellectual anomaly. This is, as suggested above, a self-evident truth, which, however, is frequently sinned against, and the sinners are to be found more among the leading clinicians than among the average practitioners. Furthermore, the fact that the living organism is provided with means of self-repair does not relieve us of the duty to strive to discover and procure also artificial remedies. Evidently, Nature's store of means of repair is insufficient; otherwise there would be no suffering and no premature deaths.

Two methods of treatment competed in the past in the domain of internal medicine: the rational and the empirical. I shall not discuss them further than to say that the rational method possesses mainly negative virtues and leads essentially to inactivity. The empirical method, which satisfies its followers by the activity to which it inspires, repelled the active minds in the profession by the vagueness of its inceptions, by the tediousness of its procedures, and

above all by the unreliableness of its results. In this despair the active minds found consolation in the study of the normal and abnormal structures and constructions of the human mechanism, leaving the question of treatment entirely out of consideration; thus medicine was threatened with the loss of its essential object. Since it was generally admitted that many ailments and diseases terminate in recovery, it was evident that the animal organism must possess means and methods by which it accomplishes these recoveries. Here, then, a competent school exists where therapy could be learned legitimately and efficiently. With this object in mind, the methods of self-repair of the animal body became the object of profound scientific studies, and immunity became the third method of therapeutics. This statement deserves to be especially emphasized. The study of immunity means the study of the natural therapeutics of the body with a view of employing it also artificially and, when possible, improve upon it. From this point of view immunity is the most rational and most promising method of therapeutics. I am afraid that this aspect of the studies of immunity is not yet appreciated even by some leading pharmacologists.

The difficulty with which these new studies were confronted was to discover and discern during the process of a disease the phenomena which were manifestations of repair. All recognizable phenomena had already their assigned places; they were pathological if they were not physiological; all deviations from the normal were parts of the disease. It was a good fortune that the antitoxins were discovered; here was something which physiology could not claim as its own, and pathology had not yet laid hands upon. Here was something which the body in its effort of defence and repair evidently manufactured anew. And I may add that here the new therapeutics was quick enough to learn to improve upon the body's method: to provide with passive immunity when active immunity failed. The new field is rapidly growing larger. Besides the discoveries of new substances and processes, many old phenomena are now reclaimed from pathology in behalf of the domain of self-repair. To quote a few trivial instances: pains of joints or muscles are looked upon as a means of insuring immobility of the diseased parts; cough is a means to remove irritating, infecting, or obstructing agencies from the air passages; the production of mucus in gastric ulcer is a means of protection for the denuded tissues from digestion by the gastric juice; vomiting or diarrhoea is a means of relieving the gastro-intestinal canal from corroding or intoxicating substances.

The present conception of the pathology of inflammation is an instructive and interesting illustration of the point under discussion. Tumor, rubor, calor, and dolor were the old insignia of inflammation. The modern pathological studies distinguish local and general symptoms. The local symptoms consist of hyperemia with

stasis, emigration of leukocytes, exudation of lymph, increase of glandular secretion, proliferation of tissue cells, and formation of granulation tissue. Of the general symptoms, we should mention only fever and leukocytosis. All of these symptoms were considered as manifestations of the disease. The present tendency in pathology is to consider every symptom as a manifestation of the efforts of the organism for defence and self-repair. The profusion of blood and lymph, with their natural bacteriolytic, antitoxic, and anti-fermentative properties; the leukocytes, with their phagocytic and digesting activities, and the lymphoid and granulation tissues, with their mechanical and vital powers, attempt to destroy and remove, or at least to wall off, the primary causes of the disease, to neutralize the secondary intoxications, to separate, dissolve, and remove necrotic tissue, and to start regenerative processes. Of the general effects, leukocytosis is now generally acknowledged as being a strong means of defence. Fever, so far as the elevation of temperature is concerned, was considered at various epochs of the history of medicine as a sign of the body asserting itself against the disease. It is now assumed by some writers that it assists in some way or other in the termination of the infection. In short, all the signs of inflammation are now considered as factors in self-repair.

It is interesting to observe how, on the basis of this newest conception, some of the very same signs which were previously considered as essential manifestations of the disease are now artificially produced for therapeutic purposes. There is to be mentioned, in the first place, the production of venous hyperemia in the treatment of various acute and chronic diseases of the body, the so-called Bier's method. The results seem to be excellent indeed. Here we see a brilliant surgeon developing a practical medical method of treatment on the very basis we have been discussing here: the therapeutics of self-repair. I call it a medical method, because it requires no knife and no anesthetics, and should be learned and employed by every practitioner.

The various attempts to influence favorably the course of infectious diseases by the artificial production of leukocytosis is another venture to utilize therapeutically one of the methods of defence and self-repair employed by the body against the cause of inflammation. As examples, may be mentioned Landererer's method of treating tuberculosis by intravenous injections of hetol; Löwy and Richter's experiments upon the production of leukocytosis by pilocarpin, spermin, and albumose-like bodies; Mikulicz's attempts to increase the peritoneal resistance to postoperative infections by the injections of nucleinic acid, as a leukotactic substance.

Fever is another means of repair which is now being tried by various investigators as a curative agent. Here may be mentioned Buchner's experiments to cure anthrax by fever brought on by injections of sterilized emulsions of Friedlander's pneumobacillus;

Dehio's method of treatment of lupus by fever produced by albumoses; and Bier's attempts to produce curative fever by the intravenous injection of alien blood.

Finally, we have to mention the recent interesting experiments of Opie, in which tuberculosis of the pleura and lungs of dogs was cured or greatly mitigated by the intrapleural injection of sterile pus obtained from another animal. It is again the therapeutic employment of a phenomenon of self-repair occurring in the local process of inflammation, namely, the phagocytic and proteolytic cell activity of the emigrating leukocytes.

I have dwelt upon the phenomena of inflammation at greater length because they illustrate the modern tendency in pathology to look upon some of the pathological manifestations as Nature's efforts for self-repair, and at the same time show the tendencies of our day to learn in therapeutics from the methods employed in Nature.

With regard to the latter, I wish, however, to append here a few qualifying remarks. In the first place, learning the methods of Nature should not imply that we have to follow them blindly; on the contrary, we ought to try to improve upon them. Nature's methods of repair often lead to disastrous results; I need only refer to strictures of canals following the natural repairs; or to the formation of abscesses in important organs without the possibility of a spontaneous innocent outlet. In studying self-repair, we need only to get the hint as to Nature's methods; but he is a bad pupil who does not try to do better than the master.

Furthermore, even if we acknowledge that certain phenomena of disease are Nature's methods of repair, it does not follow that we are bound to tolerate their continuation in all cases. In some instances we are at liberty to assume that the method is wrong and that the treatment might be even worse than the disease. For instance, even admitting that pain in articular rheumatism is a part of repair by thus insuring the immobility of the joint, we need not and should not accept this method of treatment. Immobility can be better attained by a splint, and we should, therefore, relieve the pain by an opiate or by a salicylate. Or, to take another instance, even if it be true that fever may be beneficial in some cases, it is wrong to permit its excess when it obviously makes the patient feel miserable. Besides, we should not be orthodox, and should not sacrifice the patient's comforts to mere theories. I am not willing to accept Nature's advice to treat the disease by fever to the great discomfort of my patient, as I am not willing to treat the fever with the cold bath, when, to use Osler's description, the patient is in dread of it, and pitifully begs to be left in the warm bed. We ought also to bear in mind that our duties differ from the self-imposed task of Nature. Nature strives only to avoid death; the physician has an additional duty, and that is to make life bearable. Furthermore, we should not lose sight of the fact that relieving from suffering may mean much more than symptomatic treatment; in some cases it may mean saving life. I

need only refer to one well-known fact, that general or local anesthesia may save life by avoiding shock. The recent statements that the fatal effect of anaphylaxis can be obviated by ether or chloral anesthesia contain, to my mind, a very significant principle, which should not be lost sight of in therapeutics.

Without dwelling on the subject further, I wish to emphasize my view, that phenomena of disease, when they cause serious discomfort, ought to be treated, even if they belong to the group of self-repair, provided, of course, the treatment is not endangering life.

Returning to the methods of repair of the animal body, we may say in general that the living organism responds with a reaction to any change in its normal condition; the reaction may be local or general, or both, and it may be in the nature of an increase of the normal forces, or a change in the distribution of forces; or a call upon the reserve or the latent forces; or, finally, the reaction may consist in the creation of entirely new forces.

The phenomena of inflammation illustrate the several varieties of the first-mentioned reactions. New creations are the antitoxins, bacteriolysins, anti-endotoxins, agglutinins, precipitins, and coagulins. These phenomena have been recognized only within recent years, and it is entirely premature to assume that the above list represents all the new substances which the organism is capable of producing in its struggle against disease.

The therapeutics which is based upon this new lesson from Nature has already attained great success. I need not speak of diphtheria antitoxin; its usefulness is beyond doubt. Last year's experimentation established the practical efficiency also of an anti-endotoxin. I mean the serum for meningitis. It is my impression that its practical efficiency is as good as that of the diphtheria antitoxin, if not better. The other methods of treatment by passive and active immunizations I need not dwell upon, as they will be treated by another speaker.

The enumerated instances will suffice to prove my contention that the fact of spontaneous recovery of the organism from disease can be, and has already been, utilized with great profit in favor of scientific and practical therapeutics.

The fact of spontaneous recovery has frequently, as stated above, been utilized as an argument against the use of any artificial treatment; and if the usefulness of any treatment was admitted, it was that of physiological therapeutics; that is, to improve during disease the conditions which the body requires during health. In the foregoing we have learned that there are methods of treatment which, in contradistinction to the term physiological therapeutics, may be designated as pathological therapeutics; that is, the employment of methods of treatment along the lines which the organism institutes during disease in its efforts of defence and self-repair. Pathological therapeutics promises to be the most efficient method of studying therapy.

**SAFEGUARDS OF THE HEART-BEAT.**

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THE student of disease loses nothing in accuracy and may gain much in comprehension by pausing now and then to contemplate the principles involved in phenomena that are trite and familiar. Thus, to preserve the equilibrium of the upright body there is a single physical condition which is all-essential, namely, that a vertical line dropped from the centre of gravity of the body shall pierce the area circumscribing the feet. Let the frame be bent to any extent in one direction, equilibrium may still be preserved by a definite mechanical displacement in the opposite. Whether the area of support be large or small, the distortion of the figure great or little, the body will still stand provided its centre of gravity remain within the area of support.

What is this but *compensation*, which secures the realization of a purpose by maintaining the balance of opposing forces? Turning to the almost infinitely complex system of units of matter and energy whose equilibrium we know as Life, we always find that a departure from a mean in one direction is accompanied by a corresponding deviation in another; so that the terms "health" and "disease" find their best definition, not according to some specific adjustment of structure and function, but according to the efficacy of the balancing of ever-shifting forces by which life is maintained. We are wont to think of compensation in vital activity as some unusual adjustment to meet a critical functional failure; whereas, probably every physiological feat accomplished manifests the balancing of equal and opposite forces. The principle here involved is perhaps the main factor in biogenesis, but, nevertheless, students are prone, especially on the clinical side, to neglect its application.

While we must ascribe most adjustments of living structures to environment to slowly acting natural selection, the history of a single individual may prove the intimate dependence of growth upon physical conditions. Thus, Babak<sup>1</sup> has shown that the external gills of amphibian larvæ grow luxuriantly when the animals are kept in water poor in oxygen, but attain progressively smaller dimensions when the oxygen pressure is increased; that is, the oxygen-absorbing organs wax or wane in volume in order that the tissues they supply may receive the needed complement, no more, no less, of the vitalizing element. To the same physiological category belongs the familiar fact that the pupil of the eye dilates in the dark and contracts in the light, whereby the sensory cells of vision escape overstimulation and appreciate feeble illumination.

<sup>1</sup> Ref. in Biophysikal. Centralbl., December, 1907, 191.

Sherrington has demonstrated that even a simple motor impulse to a skeletal muscle involves a simultaneous inhibition of the tonus of the antagonistic muscle group. The mechanisms of the body are probably all radically imperfect when measured by the demands we make of artificial instruments. Yet it will doubtless be found in every case that each dereliction from mechanical perfection is so balanced by compensations that the range of usefulness of the organ to the body is thereby positively enhanced. For example, the eyeball is commonly considered to have its analogue in the photographer's camera. But its imperfections as such an instrument would make it useless in the arts for the simple reason that its whole surface is permeable to light. But light that enters the eye by any part other than the pupil must have penetrated many bloodvessels and become red in color. Under ordinary conditions of vision, then, the retina is bathed in diffuse reddish light, except for a spot in the centre upon which falls the white light which has entered through the pupil. According to the laws of physiological contrast, the sensitiveness of the retina in this area must be kept ever keen for the complementary color to that which surrounds the central spot, and that color is green. As I have already pointed out,<sup>2</sup> the psychic effects of the verdure of Nature, the uncloying joy of its greenness, find herein a physiological basis. Moreover, it has also been demonstrated that acuity of vision, which measures the optical fitness of the eye, is preëminently keen when objects are viewed in a light of greenish tinge. When, in a sensory apparatus, we find that the most hopeless physical defects are turned into the finest uses of the instrument, we may grant, without prolonging this line of analogy, that there is overwhelming *a priori* probability that every vital organ must be abundantly provided with efficient means of circumventing disaster from the overstrains which the exigencies of living necessarily more or less habitually entail.

The physiologist has no compunction of doubt in describing the heart as essentially a force pump, the continuity of whose current implies the efficient closure of the auriculoventricular valves. It is easy to demonstrate in the excised, normal heart that the perfection of valve action should leave nothing to be desired. Indeed, on forcing water into a human left ventricle, having somewhat fatty walls, through a tube tied in the aortic orifice, I have caused the heart wall to burst while the mitral valve refused to leak. When one considers the limited range of dilatability of the cardiac cavities, the extraordinary variability of the inflowing blood current, the readiness with which the heart may be overstrained by increase of the diastolic blood pressure, and the irretrievable disaster entailed by prolonged asystole, it would seem on *a priori* grounds that there must be some

<sup>2</sup> On the Physiological Effects of Light which Enters the Eye through the Sclerotic Coat, Jour. Phys., 1884, 132.

adaptation of the cardiac mechanism, not obvious in its functional structure, by which the perils of these conditions may be averted. This is practically the conception at the basis of the epochal work of T. Wilkinson King,<sup>3</sup> who, in 1837, published "An Essay on the Safety-valve Function on the Right Ventricle of the Human Heart; and on the Gradations of this Function in the Circulation of Warm-blooded Animals." King demonstrated on a large series of mammals that when the right ventricle is distended with water introduced through the pulmonary artery, there is a reflux of fluid into the right auricle. This insufficiency of the tricuspid valve is brought about by stretching, under pressure, of the yielding wall of the right ventricle to such an extent that the valve flaps are prevented from coming into approximation. Clinicians are daily in contact with examples of "relative valvular insufficiency" occurring in patients having dilated hearts. But when, according to clinical symptoms usually relied upon, there is demonstrable leakage of the tricuspid valve, it seems a reproach of Nature to describe this as a safety mechanism, for the patient is already in desperate straits. From clinical observation as well as theoretical considerations I have long held the view that overdistention of the ventricles is guarded against by compensatory insufficiency of the auriculoventricular valves which is so frequent as to be properly classed among physiological phenomena.

The physical conditions of the cardiac circulation are such as presumably to permit extensive regurgitation from either side of the heart without notable functional disturbance. Each auricle receives its blood stream under a low head of pressure from a reservoir having a capacity many times as great as the chamber which it is to supply. The walls of these reservoirs, the pulmonary veins and capillaries for the left auricle, and the venæ cavæ and their branches for the right auricle, are peculiarly extensible. These channels are capable of accommodating, probably without very notable increase of intravenous pressure, an amount of blood much in excess of that usually contained therein. The term "reservoir" which has of late frequently been used to designate these vascular territories is really descriptive of their function. It is to be expected that any backflow from the heart which does not so raise the venous pressure as to impede the circulation in the vital organs, may be tolerated without producing physiological disturbance. It may, perhaps, also be assumed that at the beginning of a given systole, the regurgitation of an amount of blood which is very small in proportion to the capacity of the venous reservoirs, might save the heart from dangerous overstrain; and toward the end of systole such backflow could prevent accumulation of residual blood. It is obvious that these considerations present a theoretical means of protecting the heart against overstrain during a temporary excess

<sup>3</sup> Guy's Hospital Reports, 1837, II.



of inflow without in any way interfering with the work of other organs; in other words, such regurgitation from the ventricles would represent a true "safety-valve" action of the auriculoventricular leaflets. As will be pointed out later, it is to be expected that such valvular insufficiency would altogether escape ordinary observation because the amount of blood thus injected into the auricles and veins is not sufficient sensibly to distend them. But when the back-flow through the auriculoventricular valves persists, the excess of blood entering the heart over that leaving it is stored up in the auricles and veins, and leads to a progressive increase of venous pressure. In such an extremity the veins are engorged and may pulsate visibly like arteries with contraction of the ventricle, because the elasticity of their walls has been pushed to the limit. The heart is now permanently dilated; the auricles may be fixed in paralytic distention, and the atrial rings are so stretched that their valves are relatively insufficient. Nevertheless, the disastrous march toward venous plethora and arterial ischemia may be checked at any point whenever the forces of compensation are able to equalize the rate of inflow and outflow of the heart. Wonderful as it seems, the physiological demands of the body may be satisfied indefinitely by a circulation maintained by a pump with radically defective valves.

Clinical observers, for the most part, appear to regard the occurrence of tricuspid insufficiency as a late link in the chain leading to heart failure—an event manifested by engorgement and pulsation of the central veins, enlargement and pulsation of the liver, and a well-marked systolic murmur audible over the precordium with maximum intensity in the tricuspid area. Gibson, however, is quoted by Babcock<sup>4</sup> as thus characterizing tricuspid regurgitation: "It is incomparably the most common of valvular lesions, and the reason this fact is not brought out in statistics upon the relative frequency of valve defects is to be found in the circumstance that incompetence of the tricuspid valve does not in itself seriously impair the general course of the circulation, and it is therefore often found among those, who, although under treatment for various affections, have no cardiac symptoms. It accordingly escapes observation unless especially sought for." Babcock deprecates this statement of Gibson's which is, however, quoted here because it expresses exactly the conclusions to which my own clinical studies have led. The class of cases which affords the evidence for this belief is one in which there are usually no subjective symptoms and few of the classic signs of cardiac disorder. In fact the subjects have not heart disease, as a rule, but only the functional expression of cardiac overstrain. There is often even no complaint of shortness of breath on exertion. A systolic murmur, usually faint and soft, with much the quality of the normal inspiratory sound in the lungs, is often heard

<sup>4</sup> *Diseases of the Heart and Arterial System*, 1903, 342.

with greatest intensity along the lower left border of the sternum. But the auscultatory signs in this region are too various and uncertain in origin to permit of diagnosis by the murmur alone. Careful outlining of the heart by percussion usually shows the area of dulness to be somewhat increased to the right, but this sign is by no means distinctive of valvular insufficiency.

In an admirable series of experiments, Roy and Adami<sup>6</sup> long ago studied the time relations of movements in various parts of the dog's heart. They compared the movements of the cardiac wall with those of the papillary muscles by means of tracings obtained from levers attached to hooks, one of which was plunged into the surface of the ventricle and the other inserted through the edge of a mitral valve.

Their records show that at the beginning of ventricular systole, during the period of "rising tension," the edge of the valve is forced somewhat into the cavity of the auricle, but that the terminal act of ventricular systole is marked by a sharp downward jerk of the valve as the wave of contraction invades the papillary muscles; and it is, according to them, this sudden increase of tension which throws open the aortic valves. Forewarned of the danger of depending upon *a priori* arguments, we may still assume provisionally that, were the wave of contraction to fail to involve the papillary muscles, these bands would be stretched like elastic cords, and, as the ventricular parietes approximate in systole, a leakage through the up-pushed valve should be expected. It is evident that the period in the cardiac cycle at which such regurgitation would occur might either cover the whole period of ventricular contraction, or be limited to the early phase thereof in case the contraction wave progressed with unusual slowness, or it might be restricted to the end of the ventricular outflow in case the contractile tonus first abandons the papillary muscles. Tracings of the venous pulse suggestive of the latter condition are obtained with great frequency. My conception of functional contraction failure of the papillary muscles was suggested by the analogy of results obtained many years ago in experiments upon the skeletal muscles. When a lever is laid over each end of a frog's muscle, which is fixed at one extremity and rests upon a horizontal support, the contraction wave, started at one end of the muscle by a submaximal stimulus, is found to diminish progressively in height as it traverses the fibers. As the stimulus is weakened the wave involves less and less of the length of the fibers. When a third lever, in connection with the free end of the muscle, registers its shortening, it is found that the length of the latent period of contraction varies inversely with the strength of the stimulus; that is, the greater the length of the inert elastic tissue that is interposed between the contracting moiety of the muscle and the lever, the more time it requires

<sup>6</sup> Heart-beat and Pulse Wave. Practitioner, 1890.

to bring the inactive part of the muscle into tension sufficient to lift the weighted lever.

The analogy between these results and the facts of cardiac activity is not far to seek. Physiological experiment on the excised heart muscle shows not only variability in the rate of progress of the contraction wave, but, at least in cold-blooded animals, an extraordinary tendency for the contraction, started at one end of a bundle of fibers, to die out before it reaches the other. The clinical phenomenon of "heart block" is sufficient evidence that somewhere in the contractile chain a conducting link is defective.

Students of the heart-beat have generally been impressed with a something like specificity in the functions of the papillary muscles. In another place<sup>6</sup> certain evidences in this direction are thus presented: "J. G. Adami," summarizing the results of experiments made by Roy and himself on the dog's heart, speaks of the contraction of the papillary muscles as 'virtually independent' of that of the ventricular wall. 'The more we have studied the tracings obtained under various conditions, the more we have been led to conclude that the moment when they begin to contract is not primarily dependent upon the moment of commencing ventricular contraction. We find, for example, that an overdose of liquor strychninæ may lead to complete asynchronism between these two components of the ventricular action; or, again, there may be a ventricular systole unaccompanied by papillary contraction, or vice versa. Fenwick and Overend<sup>8</sup> studied the contractile movements of the papillary muscles and apex of the excised heart of the rabbit. They found that the papillaries began their contraction later than the apex, and they state: 'We never observed a difference as regards the commencement of the curves of less than one-twentieth of a second. The papillaries, however, speedily lag more and more behind the ventricles until they cease altogether.'"

Haycraft and Paterson,<sup>9</sup> in repeating these experiments, find that in the fresh heart the papillary muscles contract simultaneously with the ventricle. Later the papillary muscles may begin to contract before or after the ventricular wall. Fenwick and Overend continue: "It is well known that these muscles [the papillaries] are particularly prone to all forms of structural degeneration, and that their condition constitutes the most delicate index of the general state of cardiac nutrition. In fact they might be termed the 'cardiac extremities,' since, from their single attachments to the ventricular walls, they must necessarily derive their entire blood supply from the nutritive

<sup>6</sup> On the Clinical Relations of the Papillary Muscles of the Heart. Philadelphia Monthly Med. Jour., September, 1899.

<sup>7</sup> On the Action of the Papillary Muscles of the Heart. Proc. Cambridge Philosoph. Soc., vii, part II.

<sup>8</sup> Report on the Contraction of the Papillary Muscles, and its Relation to the Production of Certain Abnormal Cardiac Sounds. Brit. Med. Jour., 1891, i, 1117.

<sup>9</sup> The Time of Contraction of the Papillary Muscles. Jour. Phys., 1896, xix, 262.

vessels which enter at their bases. In short, their circulation must be of a terminal character. It is, therefore, obvious that the *musculi papillares* are at the outset even structurally predisposed to exhaustion and degeneration, and any condition which tends to lower the nutrition of the heart as a whole must affect them with a magnified degree of intensity."

In reflecting on the feasibility of obtaining experimental evidence of functional tricuspid insufficiency, it seemed probable that clinical studies of the jugular pulse might furnish the desired facts. From the very nature of the conditions assumed to underlie such circulatory failure, it is manifest that the clinician and not the physiologist can find ready at hand appropriate material for observation. At the very outset of these studies I was astonished at the unexpected wealth of material presented in the persons of patients whose hearts would pass as perfect to ordinary clinical examination. One easily becomes convinced that the vascular movements of the neck are concerned much more prominently with changes in the veins than in the arteries. The observations can usually only be made while the subject is in the recumbent position. When this posture is assumed, a rapid, more or less, dicrotic undulation of the skin above the inner ends of the clavicles is common and signifies variations in the volume or tension of the great vessels beneath. But, to one who has not definitely investigated the subject, it will cause surprise with what frequency the external jugular veins themselves become prominent and actively pulsate.

With a stethoscope applied to the heart, it is plain in this class of "normal" subjects that the swelling of the external jugular vein usually begins just before, and reaches its acme during the first sound of the heart; it is common, perhaps usual, for the blood wave to distend the vein with a dicrotic motion. When a jugular vein is clamped by finger pressure high in the neck, it drains more or less completely. A pulsatile filling of the vein under these conditions seems to postulate a true systolic regurgitation from the auricle or ventricle rather than a mere rhythmic interruption of the stream which normally traverses the vein. But more commonly it occurs that the swelling and pulsation of an external jugular vein completely disappear when the vessel is occluded above; therefore, the important conclusion is deduced that *venous pulsation does not necessarily predicate the translation of blood mass from below, but only that of a mechanical impact*. Not infrequently, with each heart-beat the neck swells laterally along the course of the carotids. That this slow wave is due to engorgement of the internal jugular trunks and not to arterial pulsation seems proved by the fact that it ceases if the fingers are pressed gently down behind the inner end of the clavicle; at the same time the external jugular vein on the same side becomes turgid and its pulsation ceases. The pressure has simply blocked the communication between the jugular branches and the heart without interfering with the

carotid blood flow, which still may transmit its abrupt pulse wave to the tissues.

Graphic tracings may be made of these various pulsations. When the transmitting tambour is placed over the carotid artery under the angle of the jaw, the tracing obtained closely resembles the sphygmogram of the radial pulse. When the tambour is applied to the area of undulation above the clavicle, the record may still have the characters of the arterial sphygmogram or it may take on quite a new form, that of the venous pulse.

According to Mackenzie<sup>10</sup> the occurrence of a venous pulse always indicates a certain degree of cardiac insufficiency and "limitation of the field of physiological response," recovery from which depends upon the degree of overstrain to which the myocardium has been subjected. In certain cases it can be noticed that a typical venous pulse tends to assume the arterial form after the subject has taken a few deep breaths. With the registering apparatus usually employed, the venous pulse is found to be made up of a group of three characteristic waves (*v*, *a*, *c*, Fig. 1), a special discussion of which is not intended here.

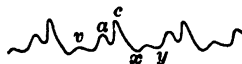


FIG. 1.—Typical venous pulse. The depression *x* marks the extreme relaxation of the auricle, and *y* the corresponding state of the ventricle.

The *a* wave is admitted to be synchronous with the contraction of the auricle and to be caused by it. The *c* wave is synchronous with contraction of the ventricle, though the cause of its formation is in dispute. When the levers registering the venous and the carotid pulse are placed in the same vertical line on a (travelling) smoked paper, it is found that the *c* wave begins about the period of outflow into the aorta, as marked by the ascent of the carotid tracing. The *v* wave, in the class of cases here under discussion, usually begins about the end of the period of outflow from the heart, marked on the carotid tracing by the dicotic notch. The origin of the *v* wave is ascribed by Mackenzie to the rising pressure within the auricle due to the constant inflow of blood during the ventricular systole. The sudden decline of the *v* wave is dependent upon the emptying of the auricle into the distending ventricle, after completion of ventricular systole. Among patients presenting themselves for examination on account of a wide range of functional disorders, I have been struck with the uniformity with which evidences of cardiac insufficiency could be distinguished, based both upon the nature of the symptoms and the

<sup>10</sup> The Study of the Pulse, 1902.

character of the venous pulse. I have been led to believe that functional insufficiency of the tricuspid valve is of frequent occurrence in such cases, and that it occurs without extraordinary dilatation of the heart. Objective evidence of such regurgitation is furnished by certain forms of the venous pulse. Thus, in Fig. 2, it is seen that the *v* wave has a double crest, or, rather, the wave *v* which begins just

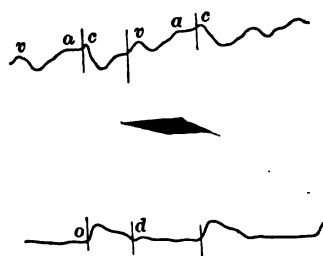


FIG. 2.—From an anemic girl aged fourteen years. The upper tracing is that of the right internal jugular pulse, showing a double crest to the *v* wave. The lower tracing is from the carotid artery; *o* is the beginning of ventricular outflow, and *d*, at the dirotic notch, marks the cessation of outflow. Events on the same vertical line in the two tracings are simultaneous.

at the moment of closure of the aortic valves, as determined by the dirotic notch in the lower tracing, is immediately preceded by a wave which is completed during the last moments of ventricular outflow. At this time the auriculoventricular valves should be firmly closed and there is no apparent reason why the gradual increase of auricular diastolic pressure, as marked by the *v* wave, should be interrupted.

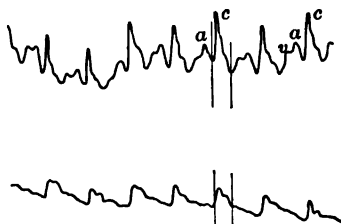


FIG. 3.—Tracings of the right internal jugular and left carotid pulses from an athletic boy aged eighteen years, who had overstrained his heart with exercise. Note the undulations on the descending limb of the *c* wave, which can hardly be due to instrumental defects.

But if we may assume that toward the end of ventricular systole the papillary muscles relax, it is obvious that the tricuspid valves might be lifted by the intraventricular pressure and allow the regurgitation of a certain amount of blood which might cause the first elevation of the wave *v*. It is obvious that the earlier in the systole of the ventricle the assumed papillary relaxation occurs, the earlier is the projected wave depicted upon the tracing; thus, in Fig. 3, the

notch on the descending limb of the *c* wave apparently illustrates such a condition. Marked insufficiency of the papillary muscles occurring early in ventricular systole might readily so reduce resistance to regurgitation that the arterial outflow would cease and the semilunar valves be closed prematurely.

The well-known variations in the height and extent of the *v* wave which depict the progress of early cardiac insufficiency are readily explained by conditions like these. These graphic symbols have their symptomatic counterpart, and, in a rather limited experience, I have been gratified with the therapeutic results of treatment directed to the conservation of cardiac energy in such cases. Mackenzie exhibits many tracings which represent the double apex of the *v* wave. In his explanation of the double crested *v* wave, he attributes the portion preceding the notch, which coincides with the terminal period of arterial outflow, to the same accumulation of blood within the auricle, which, according to him, causes the usual *v* wave, while he assumes that the portion of the wave following the notch to be due to tricuspid regurgitation resulting from the resistance to backflow into the auricle suddenly falling below that offered to outflow through the pulmonary artery. Such an explanation would involve a shortening of the period of outflow, for which there seems no evidence, and, according to pulse tracings, an extreme prolongation of the period of ventricular contraction. According to the theory proposed in this paper, regurgitation might readily occur either before or following semilunar closure or during both periods. In cases of "premature systole," with the stethoscope applied over the heart, one frequently hears a short first sound, sometimes accompanied by an obscure murmur, followed quickly at times by a second sound of semilunar closure. The radial pulse wave belonging to the short ventricular systole is usually absent, but at the moment of systole there is a sudden bulging of the jugular bulbs, which forms a striking feature of the dyscrasia. An obvious explanation of the phenomenon is that the contractile wave which seizes the ventricular muscle fails to reach the distal extremities of the fibers; the resistance to outflow into the auricle is, therefore, less than that into the aorta and, accordingly, most of the ventricular content is regurgitated. The fact that the aortic resistance, and doubtless that in the pulmonary artery as well, rises steadily from minimal to maximal pressure between the beginning and the end of ventricular outflow, may possibly determine the failure of the weaker part of the cardiac muscle toward the end of systole. Hewlett<sup>11</sup> would probably class such regurgitations as examples of the "positive venous pulse" dependent upon simultaneous contraction of auricles and ventricles. Even if these two chambers do contract simultaneously, of which there has been no evidence in the examples studied by me, such

<sup>11</sup> The Interpretation of the Positive Venous Pulse. Jour. Med. Research, October, 1907.

synchronism of action should be attended by regurgitation from the ventricle, because its systole begins while the auriculoventricular valves are still open. But, as demonstrated by Mackenzie in his chapters on irregular heart action, the venous pulse in such cases can only be interpreted in the light of an exact conception of the relative time phases of auricle and ventricle, a subject which cannot be entered into here.

Before concluding this important subject it is well to picture again the condition of hydrostatic pressure existing within the ventricle toward the end of ventricular systole. The whole mass of the organ is in strong contraction. The auriculoventricular valves are held down at an indeterminate level by the pull of the papillary muscles. Suddenly, now, the outflow through the pulmonary artery ceases and, *provided there remains in the ventricle a sufficient residue of blood*, there is just as suddenly imparted to the under surface of the auriculoventricular valve an excess of pressure proportional to the relief of strain which has been cut off by closure of the semilunar valves. It seems wholly probable that the valve should thereby be pushed more or less into the cavity of the auricle and impart to its contained blood an impulse. As has already been shown, such an impulse could give rise to a wave in the venous tracing without necessarily involving any considerable displacement of blood mass. It is most significant that the more nearly normal the subject in whom the venous pulse is recorded, the more exactly does the beginning of the *v* wave correspond with the moment of closure of the semilunar valves. Now let us conceive the course of events under conditions of weakness of the papillary muscles. The resistance to ventricular outflow increases as the systole progresses and arterial pressure rises. This heightened hydrostatic pressure is imparted to the auriculoventricular valve, producing a strain whose total value is dependent upon the surface exposed. It should be expected that, were the tone of the papillary muscles to lessen toward the end of systole, still more, were the valve to become insufficient, we would find the *v* wave of the venous pulse to take its origin at a variable period preceding semilunar closure; and any sudden increase of the impulse imparted to the auricular contents, such as might be caused by a jet of blood escaping from the ventricle, could very well cause a doubling of the *v* wave such as is actually found in tracings of certain weak hearts.

From an *a priori* point of view it would seem probable that a safety-valve action of the auriculoventricular mechanism would be especially liable to occur at the beginning of ventricular systole when the ventricle is most distended and its contractile substance at the greatest mechanical disadvantage. It would seem that any undue retardation of the wave of contraction might permit such stretching of the papillary muscles as to allow regurgitation of blood during the "period of rising tension." The *c* wave, which covers most of the



period of outflow from the ventricle, should be modified by such regurgitation, but the factors entering into its production are still too uncertain to permit conclusions to be drawn from its change of form. It may be said, however, that in many of my tracings from cases of functional heart weakness, the magnification in the height of the *c* wave is very suggestive of valvular insufficiency early in systole.

The so-called safety-valve action of the auriculoventricular trap-door, whatever its significance in the cardiac economy, is generally regarded as an attribute of the right ventricle alone. If there be any truth in the proposition advanced above, that insufficiency of the auriculoventricular valve may occur through stretching of inert papillary muscles at the time of ventricular systole, there seems no reason why the same events should not, under appropriate circumstances, attend the action of the left ventricle. The anatomical fact that the tricuspid valve is suspended to a thick, circular ring of muscle, while the larger anterior flap of the mitral valve is made by a prolongation of the aortic wall, would lead to the expectation that functional dilatation of the auriculoventricular opening of the right side might easily occur, but not of the left. Tracings of the jugular pulse seem to offer experimental evidence of events occurring on the right side of the heart. One might expect that the record of movements of the left auricle, which can be obtained by connections with a rubber balloon resting in the oesophagus, should furnish certain evidence of mitral regurgitation. Yet Rautenberg,<sup>12</sup> in his observations on this subject, expressly states that in well-compensated organic insufficiency of the mitral valve the tracings of pressure changes and movements of the left auricle are almost identical with those derived from the normal subject. Yet speculation, if sharply defined as such, seems entirely excusable on so important a subject.

The distress of an enfeebled heart is, in general, determined by the strain imposed by an excess of blood in one or more of its chambers. It is manifestly important for the pathologist to know the normal variations of the intracardiac blood pressure and the reactions of the cardiac chambers thereto. There can be little doubt that the movements of respiration normally produce a rhythmic variation of the ratio of intracardiac pressure on the two sides of the heart, yet definite physiological observations on this important subject seem to be wanting.

It is admitted that the inflow of blood to the right auricle is accelerated with the movement of inspiration and retarded with that of expiration. In inspiration the vascular bed of the lungs is increased and the resistance opposed to opening the pulmonic semilunar valves is probably diminished; but the aspirating force of inspiration

<sup>12</sup> Die Registrierung der Vorhofspulseationen von der Speiseröhre aus. Deut. Arch. f. klin. Med., September, 1907.

would presumably be still more effective in retarding the blood flow into the left auricle; therefore, during inspiration we should expect an overfilled right heart and an underfilled left heart. The mechanical effect of an expiratory movement is just the reverse, and during expiration the diastolic content of the right heart would be decreased, while that on the left would be increased. An alternation of heart strain on the two sides would presumably run parallel with the degree of filling. A comparison of the curves of intrathoracic and arterial blood pressure gives general support to the foregoing position;<sup>13</sup> but the temptation to build upon even the most plausible theoretical notions is counteracted by the advance knowledge that the only trustworthy conclusion is to be reached by exact experimentation.

It is very desirable that we should have at hand means for the clinical estimation of the changing relations of heart strain. There is reason for supposing that such a means is to some extent provided in the *physiological* reduplication of the heart sounds.

These reduplications, whatever their cause, are synchronous with definite phases of respiratory movement. I have elsewhere pointed out<sup>14</sup> that a splitting of the second sound at the base of the heart, beginning early in inspiration and increasing in interval to the end of the movement, is a perfectly normal phenomenon. Reduplication of the first sound of the heart at the apex, although somewhat less frequent, is still extremely common. Potain long ago showed that this doubling is usually confined to the end of the period of expiration. I have already discussed this subject at length, concluding that reduplications of the first sound of the heart are a sign of somewhat excessive, but still physiological, heart strain.

Clinical observation shows that the reduplication of the first sound at the apex is usually heard only in the erect position. When the subject lies supine the reduplication disappears and is commonly replaced by a soft systolic murmur that might easily escape detection. I have ventured the opinion that the reduplication itself is due usually to a late contraction of the papillary muscles of the left ventricle causing a corresponding and isolated sound of valve-tension, and that *the systolic murmur in the recumbent position is due to a real valvular insufficiency from imperfect papillary contraction*. Although the evidences for this conclusion are far from satisfactory, they seem to harmonize from different points of view. If crucial proof of the correctness of the suggestion can ever be furnished, a common "safety-valve" action of the mitral mechanism will have been established. The *a priori* probability that the right ventricle, at least, is provided with the capacity for a safety outflow within the range of physiological action is greatly strengthened by

<sup>13</sup> Foster's Physiology, 4th ed., 364.

<sup>14</sup> The Clinical Significance of Reduplication of the Heart Sounds. AMER. JOUR. MED. SCI., 1898, cxvi.

the clinical study of persons who manifestly suffer from functional insufficiency of the heart and in whom tracings of the jugular pulse furnish the most constant objective sign of the cardiac weakness.

We turn now from a consideration of the problematical functional insufficiency of the auriculoventricular valves, the purpose of which in the economy must be to save the ventricles from overstrain, to a similar provision looking to the safety of the auricles. Admitting that the so-called "negative" venous pulse may at times have its origin in mere rhythmic intermission and acceleration of blood flow into the right auricle, there seems in many cases no doubt of the truth of Mackenzie's contention that even the "negative" or "auricular" form of venous pulse represents imperfect closure of the mouths of the great veins at the time of auricular systole, allowing regurgitation of blood from the contracting auricle. The important conclusion, deduced by Mackenzie from his clinical studies, that the existence of such a venous pulse always postulates a "limitation of the field of response" of the heart, almost necessarily carries with it the corollary that even the lighter forms of venous pulse are manifestations of a *compensation* through which overstrain of the delicate auricle is prevented through backflow into the capacious "venous reservoir." A consideration of the conditions in compensated mitral disease leaves little doubt that the left auricle enjoys, at least, as efficient a protective outlet as the right.

In conclusion, while admitting the lack of the essential crucial evidence for the positions assumed in this paper, the physician in his practice must often act with less secure support. Strength has been added, I trust, to the conception that regurgitation from the auricles, thus preventing overstrain, is an occurrence so frequent that it cannot be regarded as a pathological event. Also, the indications are unmistakable that regurgitation from one or both ventricles, not caused by excessive dilatation of the auriculoventricular rings, but due to valvular insufficiency produced in another way, is an early and habitual sign of heart weakness. The therapeutic importance of the recognition of such signs of enfeeblement hardly needs an advocate.

**CARDIAC ARRHYTHMIA.<sup>1</sup>**

FROM A PRACTICAL STANDPOINT, IN THE LIGHT OF RECENT  
INVESTIGATIONS.

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BEFORE entering upon a description of the various forms of cardiac arrhythmia it may be profitable to review hastily a few of the basic tenets of the myogenic theory of cardiac activity, since the modern studies of arrhythmia are based upon this conception. The myogenic doctrine maintains that the rhythmic contraction of the heart is due primarily to inherent properties of the cardiac muscle, and relegates to a position of secondary importance the nervous and chemical stimuli which doubtless play a part in the regulatory mechanism.

The heart muscle possesses five distinct properties, which may vary independently of each other: automatic stimulus production, conductivity, irritability, contractility, and tonicity. By *chronotropic influences* are meant those which influence the production of motor stimuli; when positive they accelerate stimulus production, shortening the time required, and thus increasing the rate; when negative the opposite effect is produced. When primary, stimulus production is accelerated directly, when secondary, the results are brought about through changes in irritability or conductivity. *Dromotropic influences* affect conductivity; *bathmotropic*, irritability; and *inotropic*, contractility. For example, stimulation of the pneumogastric nerve produces arrest of the heart. This may result from cessation of stimulus production (primary negative chronotropic influences), or through depression of excitability (primary bathmotropic influence), or to the fact that the stimulus though normally generated and received is not conducted (negative dromotropic influence).

The heart muscle has the ability to generate rhythmic stimuli, the nature of which is at present unknown, though a chemical character has been suggested, and not without strong reason, for recent experiments have demonstrated the necessity of certain inorganic salts in the maintaining of heart rhythm. Normally these stimuli arise in the venous ostia of the right heart, and pass downward through the bundle of His to the ventricles, not, however, as the result of nervous conduction, but by reason of muscular continuity, from cell to cell (Gaskell, Engelmann). Stimuli, however, may be generated at

<sup>1</sup> Read at a meeting of the College of Physicians of Philadelphia, April 1, 1908.

other points, but under normal conditions they are not of sufficient intensity to interfere with the rhythm, as may be the case pathologically, when the route of conduction may even be reversed. The left auricle, however, seems to have no power of automatic rhythmicity. The wave of contraction passes through different parts of the heart at a varying rate, a condition which favors a more complete ventricular systole (Engelmann). Stimulus production and conduction, as well as contractility, are much influenced by the phase of the cardiac cycle, the function of each being depressed during systole, and gradually restored during diastole. All these functions may vary in activity, independently of each other; they are also much influenced by the pabulum supplied by the arteries and lymphatics, by the removal of waste products through the veins, and by nerve impulses. Stimulation of the vagus depresses stimulus production, conductivity, and contractility. Stimulation of the accelerator nerve has the opposite effect. The vagus acts very slightly if at all on the ventricles, except indirectly through the auricles (Erlanger). In complete heart block the administration of atropine, though increasing the auricular rate, will have no effect on the ventricular rhythm (Gibson and Ritchie). Heart block itself may result from vagus action; this, as has been shown by Mackenzie may occur during deglutition. Conductivity is depressed by asphyxia; and when this function is below par the administration of digitalis still further increases this depression, a practical fact of great clinical importance to which I shall again allude.

From the foregoing brief review it is easy to see that in order to explain satisfactorily and study the different forms of arrhythmia we must first reduce them to their simplest terms, so to speak—that is classify and group them according to whichever one of the five fundamental properties of the heart muscle is chiefly or entirely concerned in their production.

Experimental physiology has made such rapid strides of late years that it is well nigh impossible for the general practitioner of medicine to keep pace with its latest developments, but our knowledge of the physiology of the circulation has undergone such extensive and important basic changes of late (through the labors of Gaskell, His, Erlanger, Engelmann, Hering, Mackenzie, Cushny, Wenkebach, and others), changes which are daily receiving corroboration and endorsement, that the physician can no longer afford to be uninformed of at least their fundamental principles. The myogenic theory of cardiac activity, while not as yet accepted by all physiologists, is daily gaining adherents. Although it doubtless still requires an enormous amount of investigation and revision, nevertheless, it elucidates satisfactorily and with such minute exactness so many hitherto unexplainable conditions, such as Adams-Stokes disease, extrasystolic arrhythmia, etc., that its acceptance as a working basis is practically necessitated. It was in a very similar

manner that Wasserman's theory regarding the blood complement, etc., led to a much more accurate and satisfactory knowledge of the question of immunity than had previously obtained.

The first type of pulse irregularity to which I wish to call attention is:

1. **JUVENILE ARRHYTHMIA.** It is, of course, well known that respiratory activity influences the pulse. In normal individuals inspiration increases and expiration decreases the rate. Some people show this phenomenon much more than others. It is especially common in youth, and has hence been called by Mackenzie the youthful type of arrhythmia. The type of irregularity affects chiefly the diastolic period, and for this reason it is noted especially when the pulse is slowing down, after infancy, and after a febrile attack. Mackenzie found that all children at some time exhibited this symptom. It occurs most frequently between the ages of eight and fifteen years, becoming less common toward puberty. It is pathological only when induced to a marked degree by quiet breathing, or when it is not controlled by apnoea. It indicates nerve irritability and is proof of vagus activity. It occurs in fevers, especially during convalescence, in neurasthenia, and in cerebral lesions causing irritation of the vagus. Tracings taken from the precordial region show that it consists of a true intermission, and is not simply a missed beat at the wrist resulting from extrasystole. Needless to say, it has an altogether entirely different genesis than the *pulsus paradoxicus*, which is entirely due to the mechanical relations of the pericardium and mediastinum. Peters has shown that the vast majority of arrhythmias occurring during the late stages of diphtheria and scarlet fever are of the respiratory type. These two infections are so frequently the cause of serious myocardial lesions that pulse irregularities following them are naturally regarded with alarm. If, however, in such a case we are able to demonstrate a simple respiratory arrhythmia, our prognosis will of necessity be much affected by the finding.

The second group of arrhythmias which I shall consider is the one most frequently encountered, namely:

2. **EXTRASYSTOLE.** As a rule, an intermittent pulse is due to extrasystoles, resulting from abnormal irritation at some point of the musculature, generally the ventricle, although it may result from heart block or diminished excitability. These extrasystoles can often be heard on auscultation and are registered on the cardiogram, although the pulse wave may not reach the periphery. The later the extrasystole occurs in diastole the louder will be the sound heard, and the larger the pulse wave, so that if it occurs shortly before the normal time we may get the simulation of a normal, somewhat anticipated, systole. The futile contractions (*frustrane Kontraktionen*) of Hochhaus and Quinke are examples of extrasystoles occurring early in the diastolic period. Extrasystoles may

also occur without causing dropped beats or compensatory causes, in cases of bradycardia in which the refractory phase is short in comparison with the length of the pulse rhythm. Experimentally an extrasystole may be produced by increasing the *vis a fronte* in the circulation; it is also seen in digitalis poisoning, and after the administration of calcium. It may also be produced by mechanical and electrical means.

Extrasystoles are explained by the fact that as the refractory phase of the heart rhythm is coming to a close the muscle becomes more and more susceptible to stimuli. An abnormal stimulus sets off the contraction before its time, just as hot carbon in the cylinder of a gasoline engine explodes the charge before sufficient compression has occurred. As the result we see a weak, early contraction which, owing to an insufficient volume of blood and inadequate contractile force—resulting from shortened diastole—barely, if at all, opens the aortic valves. This extrasystole, however, throws the heart into a second refractory period at a time when the normal physiological stimulus should occur; in this manner a beat is dropped and a compensatory pause is brought about. By reason of the latter the number of heart beats per minute may remain unchanged despite the occurrence of extrasystoles, and the length of time occupied by the normal contraction and the extrasystole plus their respective pauses may occupy an equal interval of time as would two normal contractions. This condition of affairs is characteristic of extrasystoles arising in the ventricle. When the abnormal stimulus arises at the mouths of the veins in the right heart, the compensatory pause is absent; if in the auricle itself, it may or may not be present; if in the ventricle, it is present and is not infrequently prolonged.<sup>2</sup> But if this prolongation is great we are strongly led to suspect that the trouble is due to depression of conductivity and not to the fact that the stimulus arrived in the refractory period.

A series of extrasystoles following each other gives rise to the pulsus bigeminus, trigeminus, quadrigeminus, etc., according to their frequency, while a continuous series may produce a clinical paroxysmal tachycardia, although Hoffmann has shown that in tachycardia due to this cause a series of compensatory pauses may be distinguished.

Extrasystole is often recognized subjectively by the patient as a dropped or a doubled beat, or a powerful thump which follows the compensatory pause. It is not however, always an easy matter to determine whether an arrhythmia is or is not due to extrasystole. Thus, when the intermissions occur in different kinds of groups, with varying degrees of peripheral pulsation; when we find abnormally long compensatory pauses, and small pulses following them, we may be unable to make out the regularity of the rhythm both

<sup>2</sup> Hering, Pflüger's Arch., lxxxii; Präger med. Woch., xxvi, Nrs. 1 und 2.

in the ventricle and in the artery, despite the fact that the stimulus production may be going on normally at the venous ostia. Furthermore, extrasystoles often complicate other forms of arrhythmia, making interpretation difficult. We have the three definite varieties of extrasystoles: (1) Auricular; (2) ventricular; and (3) auriculo-ventricular; the latter two being the more common. What is known as the interpolated ventricular extrasystole is one which has but little influence on the rhythm, although it may produce a retrograde auricular systole.<sup>3</sup>

Extrasystole is seen in many conditions, which may be grouped as follows: (1) Physiological or individual; (2) after severe exertion; (3) in women at puberty, in pregnancy, and at the climacteric; (4) toxic causes: alcohol, ether, tobacco, infectious fevers, especially during convalescence, and in intestinal disorders; (5) nervous disturbances: neurasthenia, hysteria, neuroses; (6) arteriosclerosis; and (7) organic heart disease.

Clinically, extrasystoles are generally manifested as two or more approximated beats, followed by an intermission. If the extrasystole occurs early in the diastolic period, as is generally the case, we, as a rule, hear on auscultation a muffled third sound during diastole. The heart is at this time insufficiently filled with blood, the pressure in the aorta is too low, and the ventricular contractile power weak, owing to insufficient rest, as a result of which the aortic valves are not opened by the extrasystole. If the extrasystole occurs later in the diastolic period, a second sound may be produced. The extrasystole is generally followed by an unduly prolonged silence, which is, in turn, brought to a close by a strong, loud, muscular sound of the next regular systole. If the extrasystole has resulted in opening the aortic valves, a small, early pulse wave is seen on the sphygmogram—pulsus bigeminus. Rarely the tracing may simulate the normal dicrotic wave.

Extrasystoles may be induced by a number of causes. It has been shown, both experimentally and pathologically, that increased aortic blood pressure is a prolific source of this symptom. Extrasystoles are also brought about through pathological changes in the myocardium, which appear to initiate a stimulus to which the neighboring normal muscular fibers respond. Increased excitability—positive bathmotropic influences—toxic or thermic in origin, are also often productive factors. And finally, we have to include nervous influence. The latter influence is an indirect one acting through vasoconstriction, which is a well-known excitant. Extrasystoles often occur as an early sign of functional derangement in patients with obesity or arteriosclerosis, and although they may exist for years without any more serious symptoms, their presence calls for careful investigation of the case in which they appear. According to

<sup>3</sup> Hering, XXIII Kongr. f. Inn. med., München, 1906.



Hewlett, extrasystoles usually do not develop during the acute myocardial lesions of infectious diseases, but when they do appear under such conditions they are of a relatively worse significance.

The occasional occurrence of extrasystole in young, otherwise healthy individuals is of little importance. The symptom, however, always points to cardiac irritability, and while this may be normal for some individuals, its presence should always make us look carefully for intracardial and extracardial abnormalities. Anyone who has auscultated the heart in horses or dogs is aware how frequently extrasystoles occur, and how easily they are produced in these animals. Similarly there are certain individuals, notably those with highly strung nervous systems, who exhibit the symptom more or less constantly. Beyond indicating cardiac irritability, extrasystoles give us no positive clew; they are not pathognomonic of any particular disease.

Wenkebach divides individuals exhibiting extrasystoles into four groups:

1. People who live to old age without demonstrable heart lesion, who have experienced this symptom off and on for a variable period of years, without any deleterious consequences. Such cases probably result from a congenital or acquired hypersusceptibility to stimuli.

2. The extracardial group, to which class belong the toxic and reflex cases. Extrasystoles are very commonly seen during the convalescence from infectious fevers—typhoid fever, pneumonia, diphtheria, etc. They also occur as a result of the use of tobacco, alcohol, tea, and coffee; as well as in cases of gastro-intestinal disturbances, intestinal parasites, etc.

3. To this class belong those who are the subjects of circulatory disease, regardless as to whether the heart be seriously affected or not. For instance, cases with arterial hypertension frequently exhibit extrasystoles. The same may be said of arteriosclerotics. In these cases the symptom is often intermittent and readily produced by physical effort or mental excitement. Some of these cases can, of course, be explained on the basis of hypertension, but Wenkebach favors the view that the cardiac muscle becomes more irritable as age advances, for the following reasons: (a) Other signs of irritability, such as delirium cordis, are frequent in elderly people. (b) In both young and old subjects extrasystoles are of common occurrence when arterial tension is low. (c) Diseases in which hypertension is most frequent, such as chronic nephritis, are not those in which extrasystoles are most common.

4. Cardiopath. In this class extrasystoles are of frequent occurrence. We can, however, draw no definite deductions by the mere fact of their presence as to the stage, character, or extent of the heart lesion. Productive factors are present in great numbers in such cases, that is, dilatation, inflammation, local cardiac anemia, overexertion, etc. The worst cases of heart disease often terminate

fatally without having at any time exhibited extrasystoles. Wenkebach concludes: After all that has been said, clinicians ought not to attach too much significance to extrasystoles in themselves, and yet they ought to consider it worth while to examine every case and determine whether a cardiac lesion is present or not, whether there are any conditions (and they must often be looked for outside of the heart) present, which could account, directly or indirectly, for the presence of the extrasystoles.

Mackenzie, basing his views on the postmortem histological findings of Keith, states that in the majority of cases of extrasystole in the aged there are to be found minor pathological changes in the auriculoventricular bundle which can account for the depressed conductivity and hyperexcitability, although he admits that there were also present abnormalities of the coronary arteries and of the ventricular musculature.

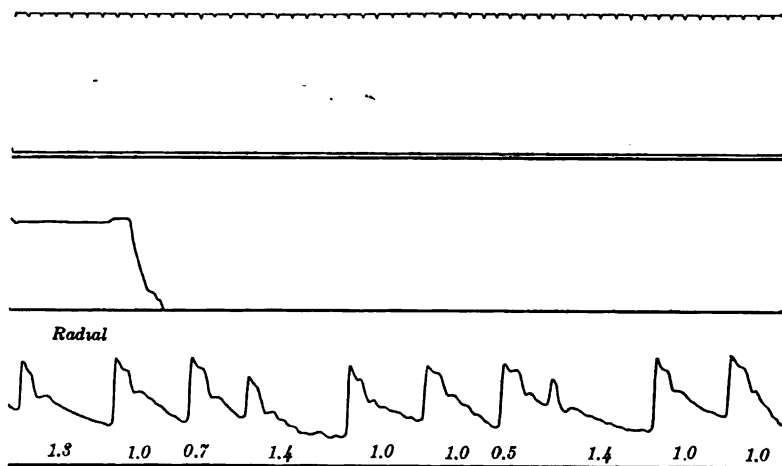


FIG. 1.—Extrasystoles of ventricular origin, followed by compensatory pauses. The normal systole plus the extrasystole occupy the same or a slightly longer interval of time than two normal beats.

The accompanying illustration (Fig. 1) shows extrasystoles of ventricular origin occurring in a patient with arteriosclerosis. It was present only temporarily after a change of posture. It appeared in the erect and in the recumbent position for a few minutes after the posture was assumed, and then gradually ceased. The systolic blood pressure was 135 mm., the diastolic 95 mm.<sup>4</sup>

Fig. 2 exemplifies the occurrence of extrasystoles of auricular origin. They are preceded by auricular (*a*) waves in the jugular tracing, and are not followed by compensatory pauses, as are ventricular

<sup>4</sup> The time recorded on all of the following tracings is in units of one-fifth of a second.

extrasystoles. This tracing was taken from a man aged sixty-six years, with a high grade of arterial thickening, and a systolic mitral murmur which completely replaced the first sound of the heart. The heart dulness was greatly enlarged to both right and left. The systolic pressure was 160 mm., the diastolic 110 mm. He complained of vertigo after any sudden change of posture, precordial oppression with dyspnoea on exertion, and improved under the administration of digitalis. There is marked delay in conductivity—the *a* to *c* interval being 0.4 instead of 0.2 of a second, indicating myocardial involvement.

Fig. 3 illustrates extrasystoles of auriculoventricular origin; in other words, the abnormal stimulus arises in the bundle of His. The large waves marked *a* and *c* are due to the simultaneous con-

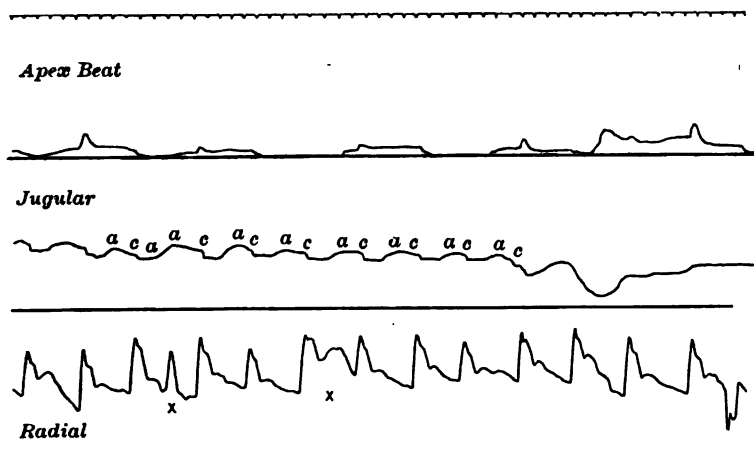


FIG. 2.—Extrasystoles of auricular origin. They are preceded by auricular waves in the jugular tracing *a*, and are not followed by compensatory pauses.

traction of the auricles and ventricles, both being premature. These waves are not followed by a *c* wave, and the diastole following is of the same length as the normal auricular rest period. This is the form of extrasystole which has been designated by some observers as the retrograde extrasystole, it being assumed that the abnormal stimulus arises in the ventricle and is transmitted backward to the auricle. This explanation is hardly satisfactory, however, for, as Mackenzie has pointed out, if such were the case there should be a delay of one tenth of a second in the appearance of the auricular wave—the time required for the stimulus to travel across the auriculo-ventricular bundle—whereas, in reality, the contraction of the auricle and ventricle are exactly synchronous.

This tracing was taken from a physician aged sixty-six years, who complained of precordial oppression, and a thumping in his chest

which occurred with each intermittence of the pulse. Physical examination disclosed a double aortic lesion. The radial pulse on

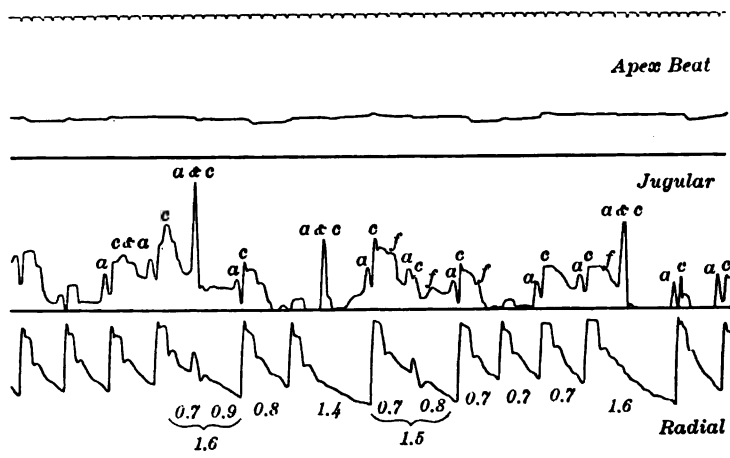


FIG. 3.—Extrasystoles of auriculoventricular origin (arising in the bundle of His). The tall waves *a & c* are due to the simultaneous contraction of the auricles and ventricles. They are not followed by *c* waves or by compensatory pauses.

the tracing shows the characteristically rapid collapse which follows the straight, high, systolic limb.

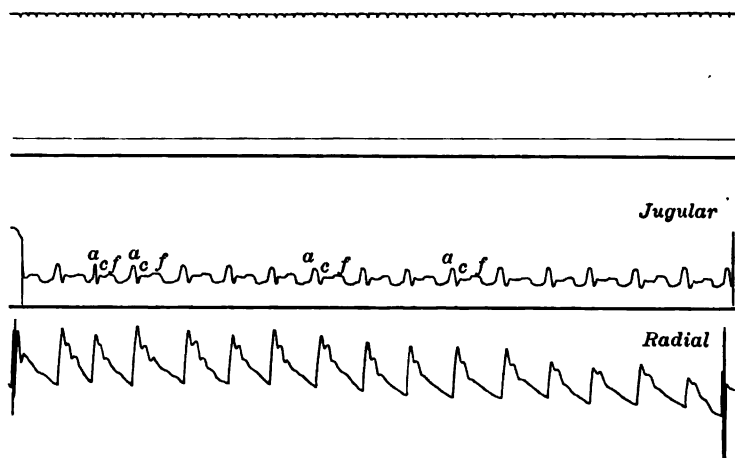


FIG. 4.—The same case as Fig. 2. The extrasystoles have disappeared. The jugular tracing shows the three normal waves.

Fig. 4 was taken from the same patient one year later. The arrhythmia had entirely disappeared. The pulse rate was 68, the systolic pressure 190 mm., the diastolic 110 mm., and the patient was comfortable and attending to his work.

Fig. 5 illustrates extrasystoles of ventricular origin, appearing early in diastole, followed by compensatory pauses, and failing to appear in the radial pulse, except occasionally, this being due to the fact that the ventricle has been insufficiently rested and inadequately filled with blood, as the result of which the aortic valves were barely if at all opened. This tracing was taken from a patient with failing compensation—a double mitral lesion, with marked cardiac dilatation; death occurred about two weeks later. On auscultation two fairly loud, close-coupled sounds were heard over the apical region, followed by only one second sound at the base (occasionally two sounds were heard at the aortic area, the second being muffled and indistinct). The pulse at the wrist was for the most part quite regular, but only one beat was felt, while two sounds were heard at the apex area. If the ventricle had been stronger we should have had a typical *pulsus bigeminus* in the radial.

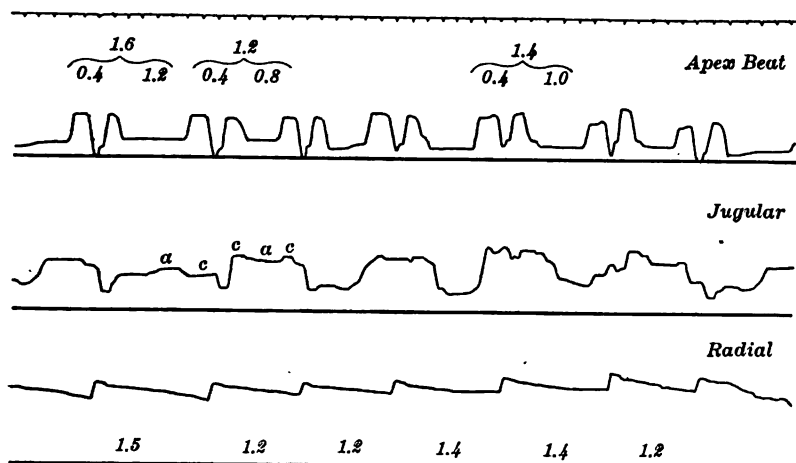


FIG. 5.—Extrasystoles of ventricular origin, which are manifest at the apex beat but do not reach the periphery. Only every other beat causes a radial pulse, thus producing a false bradycardia which without the tracing might have been construed as due to heart-block.

Fig. 6 shows a series of extrasystoles occurring in groups of two, producing a *pulsus trigeminus*, which occurred in a case of acute endocarditis, which terminated fatally about ten days later. At autopsy in addition to cardiac hypertrophy and dilatation ulceration of the aortic valves was found.

The following tracings illustrate most graphically the way in which digitalis improves the character of the pulse by suppressing the extrasystoles, producing a longer diastole, a more complete period of rest, and resulting in a greatly improved state of the circulation. Fig. 7 was taken from a case of mitral stenosis and insufficiency, with cardiac dilatation and tricuspid insufficiency. There

was general anasarca, cyanosis, orthopnoea with blood-tinged expectoration, and a pulsating liver. The tracing shows the marked

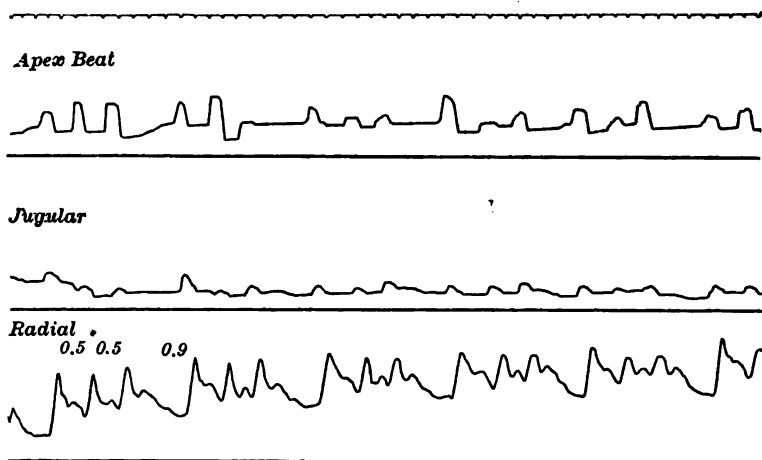


FIG. 6.—Pulsus trigeminus, resulting from extrasystoles occurring in groups of two. The jugular pulse is of the positive type—the waves are synchronous with the ventricular systole; taken from a case of mitral and tricuspid insufficiency.

arrhythmia complicated by extrasystoles, and a positive venous pulse. The patient was bled ten ounces and given three drams of the infusion of digitalis thrice daily. A few days later the general condi-

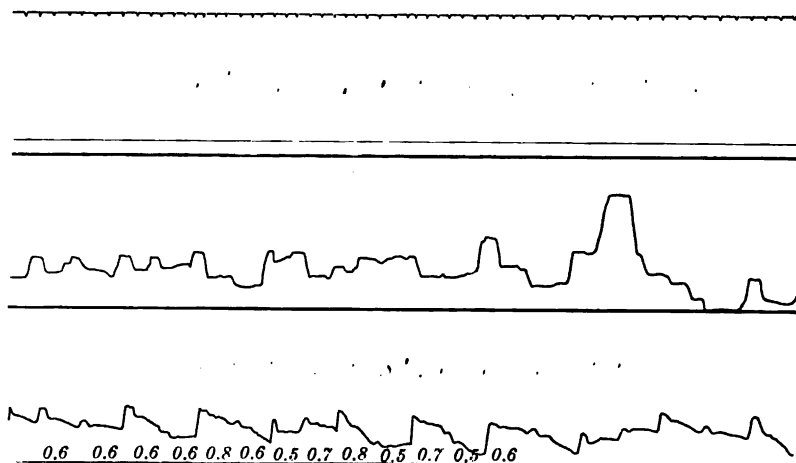


FIG. 7.—Double mitral disease with tricuspid insufficiency, showing extrasystoles and a positive venous pulse.

tion was greatly improved. At this time the second tracing was taken (Fig. 8), which shows a much slower, better filled and sustained

radial pulse, and many fewer extrasystoles. It will be seen that the jugular pulse is still of the positive type resulting from the tricuspid leakage.

The next type of pulse irregularity to which I would call attention is a variety which is met with quite frequently in the advanced stages of heart disease, generally with failing compensation:

3. PERPETUAL ARRHYTHMIA. Perpetual arrhythmia is one in which no regular rhythm whatever can be made out for long periods of time—weeks or months. The subject of its etiology requires further elucidation. When present in its typical form three characteristics are noted: (1) The jugular tracing shows no auricular wave; (2) it is always associated with a positive venous pulse; (3) absolutely no underlying rhythm can be detected. As to the second

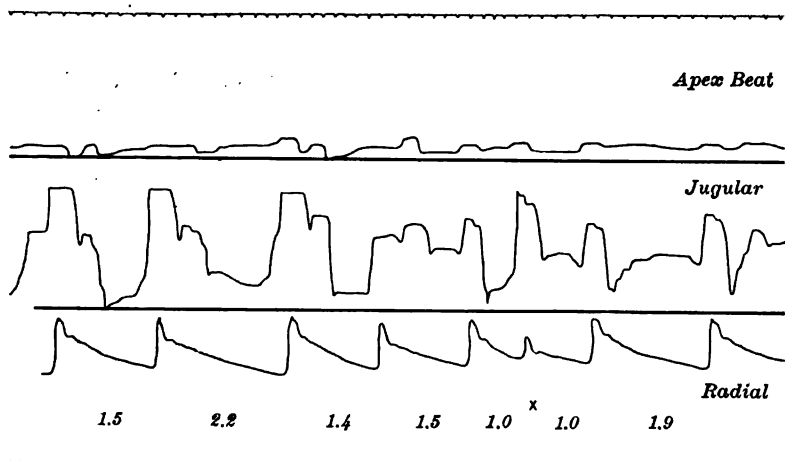


FIG. 8.—Tracing from the same patient as Fig. 7, after venesection and digitalis. Most of the extrasystoles have dropped out. There is a marked improvement in the character of the radial pulse, and there was a corresponding amelioration in the patient's condition. x, extrasystole.

qualification—the positive venous pulse—the majority of authorities hold that this is due to tricuspid insufficiency or to paralysis of the auricle. As to the etiology of this variety of irregularity, Wenk-bach believes that it is due to a block between the sinus and the auricle, the result either of muscular weakness or depression of conductivity, and not to auriculoventricular extrasystole or to pathological changes in the auricular muscle. Erlanger has recently performed some experiments which prove the possibility of an experimental sino-auricular block.

When a tracing from a case of perpetual arrhythmia is examined we are struck by the fact that no two pulse waves are of equal length. Clinically the condition is often spoken of as delirium cordis, but as Hewlett has recently pointed out, this character of pulse is sometimes met with even if the pulse is slow. We have

already mentioned the fact that a permanently irregular pulse without tachycardia or bradycardia, unaffected by respiration, digitalis, or atropine, is always associated with a ventricular venous pulse. Since auricular paralysis or tricuspid insufficiency is practically only encountered in cases with broken compensation, we find the permanently irregular pulse only in very serious cases. It is apparently always intracardial in origin, and it is often met with in arteriosclerosis and myocardial disease. Minor degrees of this irregularity may resemble the youthful type; the severer forms are often complicated by extrasystoles. The beneficial effects of digitalis in these latter forms are owing to the fact that this drug, by depressing the function of conductivity in the auriculoventricular bundle, causes a dropping out of the extrasystoles. Perpetual arrhythmia may appear and disappear either suddenly or gradually; in the latter case we often see a reappearance and steady increase in the size of the auricular wave.

Another variety of arrhythmia which has lately come into prominence as a pathological entity of much clinical importance is:

4. HEART BLOCK. This class of arrhythmias consists of those cases which are due to depression of conductivity (heart block), a condition which may exist in varying degree. It may be manifested by a dropping out of the ventricular beat or by a complete dissociation of auriculoventricular rhythm. The most marked and typical cases are those of the Adams-Stokes syndrome, in which the auricles beat more rapidly than the ventricles. It has been shown that at least the majority of these cases are due to a lesion in the bundle of His. If a sufficient number of muscular fibers in this bundle are destroyed to prevent completely the conduction of the stimulus from the auricle to the ventricle, the latter chamber initiates its own rhythm, beats independently, and a complete heart block is said to exist. If, on the other hand, every second, third, or fourth auricular contraction is able to set the ventricle in action, the condition is termed an incomplete block. Depression of conductivity sometimes occurs temporarily in the convalescent stage of diphtheria, typhoid and rheumatic fever. According to Huebner, the bradycardia, occurring after typhoid and other infections is the result of a toxic depression of conductivity. Heart block may also be produced by digitalis, and when already present the administration of this drug still further depresses the function of conductivity, and is therefore absolutely contra-indicated. This effect of digitalis is not necessarily the result of vagus stimulation, for the auricular rate may be unaffected, although the ventricular beats fail; and the pneumogastric nerve seems to act on the latter chamber only through the former. It has been shown that the pneumogastric nerve can produce not only chronotropic, but also dromotropic and inotropic effects (Muskens, Hoffmann, Engelmann). Digitalis seems to exert a specific local action on the function of conductivity.



The existence of delayed conductivity can only be determined by the coincident tracing of an arterial and a venous pulse (usually the radial and the jugular are employed). In normal cases the *a* to *c* interval as it is called—that is, the time which elapses between the systole of the right auricle and that of the left ventricle—should be not more than 0.2 seconds with a pulse rate of 70.

If this time is much increased, conductivity is impaired. If the block is complete, the auricular waves in the jugular and the carotid waves bear no constant relations to each other. Experimentation and clinical observation have shown that depression of conductivity may occur as a result of local or general anemia, of toxemia, of degeneration of the cardiac muscle, especially fibroid degeneration and myocarditis of the auriculoventricular groove. Fatigue may be a precipitating factor. I have taken tracings of a case which showed a partial block after exertion which disappeared after a few minutes rest in the recumbent posture.

Lommel has already called attention to intermittent vagus activity resulting from fatigue.

From a clinical standpoint it is important to decide whether a heart block is nervous or muscular in origin, since the former is much more amenable to treatment, and of less serious prognostic import. In attempting to determine this question we must not forget that heart block may be brought about by secondary dromotropic effect of other disturbances, such as a high pulse rate, which does not allow sufficient time for a restoration of functional activity.

In the heart block due to muscular causes the pulse rate is generally lower than in the nervous form. In the former instance the pulse is regularly intermittent, in the latter variably so, and much influenced by respiration. If the administration of a physiological dose of atropine has no effect upon the heart block, the vagus factor has been eliminated.

Heart block may occur between any two parts of the cardiac musculature possessing spontaneous rhythmicity if the bridge of connection be severed or the passage of stimulus be interfered with.

Some tracings published by Gibson seem to indicate that heart block may also be caused by depression of excitability.

Fig. 9 was taken from a case of Adams-Stokes disease. It represents an incomplete heart block with a three-to-one rhythm. The ventricle responds only to every third auricular stimulus. The function of auriculoventricular conductivity is much depressed, the *a* to *c* interval lasting four-tenths instead of two-tenths of a second. Death occurred about three months after the first attack of vertigo.<sup>5</sup>

Fig. 10 is a tracing from another case of Adams-Stokes disease, occurring in a man of middle age, who has been under observation

<sup>5</sup> Case referred by Dr. J. W. Irwin. A full account, with histological examination, will soon be published.

for three years, at which time he was admitted to the Philadelphia General Hospital complaining of dyspnoea on exertion. Tracings

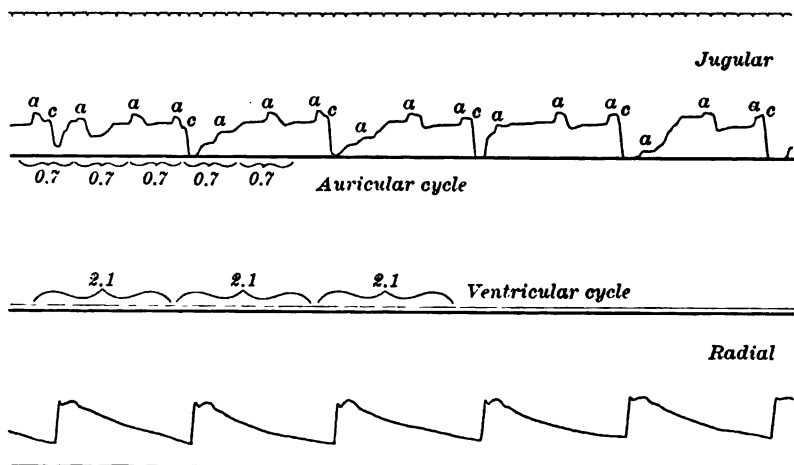


FIG. 9.—Adams-Stokes disease, with a three-to-one rhythm. There are three contractions of the auricle to one of the ventricle.

made three years ago show the same kind and degree of heart block, but since that time he has been unable to work, and vertigo as well

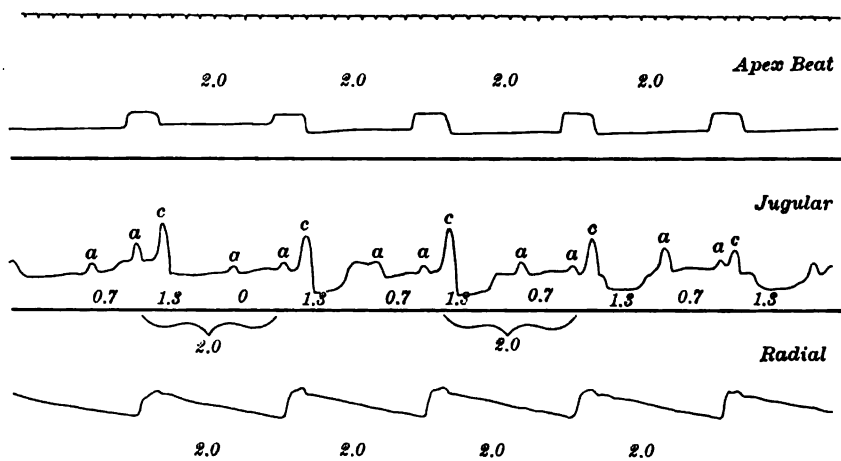


FIG. 10.—Adams-Stokes disease, with a two-to-one rhythm.

as syncope have been added to his list of symptoms.\* At the time this tracing was taken his systolic pressure was 145 mm., the dias-

\* I am indebted to Dr. F. B. Stahl for the opportunity of making the second series of tracings from this case.

tolic 80 mm. The radial pulse was 30 per minute, both erect and recumbent. It was unaffected by respiration, exercise, or the administration of atropine.

Fig. 11 is from another case of heart block with a two-to-one rhythm occurring in a man, aged fifty-eight years, who complained of dyspnoea on exertion, precordial pain radiating to the arms and head (occiput), with vertigo of slight degree. He was the subject of advanced arterial degeneration and had marked hypertension. The highest figures recorded were 235 mm. for the systolic, and 140 mm. for the diastolic pressure. At the time this tracing was taken the pressures were 150 mm. and 100 mm., respectively while recumbent, and 175 mm. and 110 mm. while erect. The radial pulse erect was 70; recumbent, 54 per minute.

It would seem, therefore, that we were dealing with a case of heart block in the early stages, since the pulse rate was still affected by change of posture. On auscultating over the body of the heart,

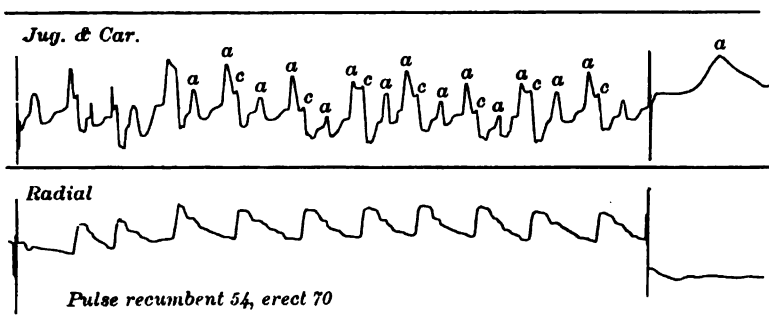


FIG. 11.—Auriculoventricular heart-block, occurring in a case of arteriosclerosis with marked hypertension and symptoms of angina pectoris. Two-to-one rhythm.

two clear, muscular sounds were heard in addition to the aortic second sound, which was high pitched, clear, and ringing, during which time only one pulse beat appeared at the wrist. Furthermore, every other auricular contraction was followed by a ventricular response. The radial pulse shows the characteristics of arterial hypertension.

Fig. 12<sup>1</sup> is a tracing taken from a man of about fifty years of age, a business man of the modern "hustler" type, in June, 1907. He complained of some dyspnoea on exertion, and an examination of the chest revealed the physical signs of aortic insufficiency, mitral insufficiency, and a dilated hypertrophy. He had lost twenty-five pounds in weight within one year, and had taken three series of Nauheim baths in this country. The radial tracing shows the typical large-waved, collapsing pulse of aortic insufficiency, with

<sup>1</sup> Case referred to me by Dr. J. H. Musser, as was also the following case.

rather well-marked dicrotic wave, perhaps the result of the mitral insufficiency. He had no fever. The jugular wave is of relatively normal proportions, and shows no evidence of auriculoventricular

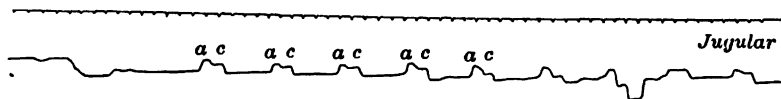


FIG. 12.—Aortic insufficiency and mitral insufficiency. Normal coördination of the auricles and ventricles is shown by the jugular pulse.

dissociation. Every auricular wave is followed by a ventricular wave. The blood pressure was 140 mm. systolic, 90 mm. diastolic. During the summer his pulse rate fell to as low as 37 per minute,

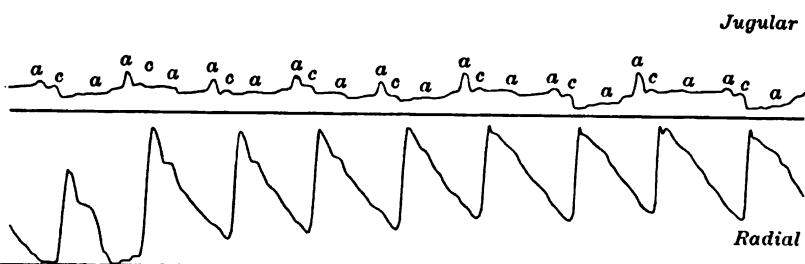


FIG. 13.—The same case as Fig. 12, taken five months later. Distinct heart-block with a two-to-one rhythm.

and for a period of six weeks remained between 37 and 40, gradually getting up to 60. During this time he felt restless and weak, but had no vertigo or syncope. On resuming his active career he found that

when physically tired his pulse would beat at 40, but that rest in the recumbent posture would, in a short time, restore the rate of 60. In November, 1907, I had another opportunity of making a pulse tracing (Fig. 13).

Here we are dealing with a distinct case of incomplete heart block, in which the rhythm varies between two-to-one, and three-to-one. The pulse rate was 48 per minute, and shortly after the preceding tracing was taken, the patient having been in the recumbent posture, returned to 60 with a disappearance of the heart block, as is shown in Fig. 14.

The last two cases described are, I believe, the first instances recorded of what with strong probability appears to be the early developmental stages of Adams-Stokes disease. How long patients afflicted with this malady may live probably varies greatly under

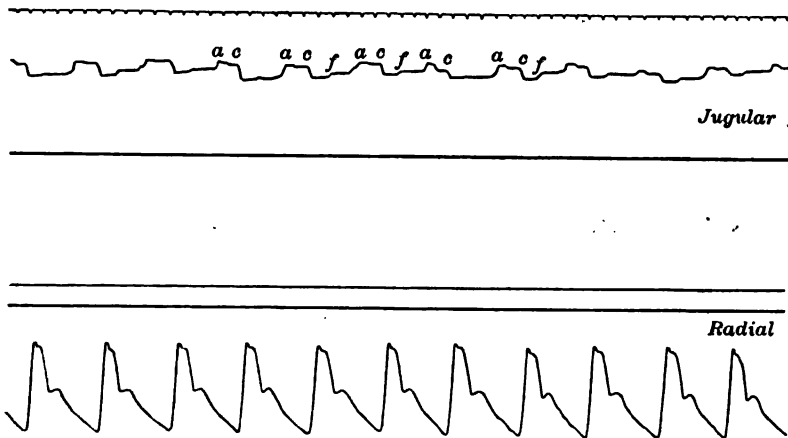


FIG. 14.—The same case as the two preceding figures, after rest. The heart-block has disappeared, and the normal auriculoventricular rhythm has been restored.

different circumstances, being dependent of course on the extent of damage done to the auriculoventricular bundle, and the character of the lesion affecting it. The case from which tracing No. 5 was taken was known to have had heart block three years ago, and doubtless had had the condition for some time before he came under observation, since his lesion has been very slow in progressing. It is more than probable that careful study by cardiosphygmographic means of many cardiopaths will teach us that heart block is a much commoner lesion than we have heretofore been led to suppose. In fact, when we consider the anatomical position of the bundle of His, it is rather surprising that it is not more frequently damaged by inflammatory processes in its neighborhood.

Fig. 15 illustrates another case of heart block due to the administration of digitalis. In this instance the pulse rate dropped sud-

denly from 80 per minute to about 40. At the time this tracing was taken it was 38.\*

The last form of arrhythmia remaining to be considered is the rarest variety, namely:

5. DEPRESSION OF CONTRACTILITY—PULSUS ALTERNANS. In this class of arrhythmias are placed the cases which are inotropic in origin; that is, those due to depression of contractility. Contractility is easily measured, since cardiac contractions are always maximal if the stimulus provokes any contraction. They are characterized by the alternate appearance on the arterial syphgmogram of a large and a small wave, either with or without increased pulse rate. True cases of this condition are not the result of extrasystole, since they are not followed by compensatory pauses, nor are they due to depression of conductivity, as can be determined from the jugular tracing;

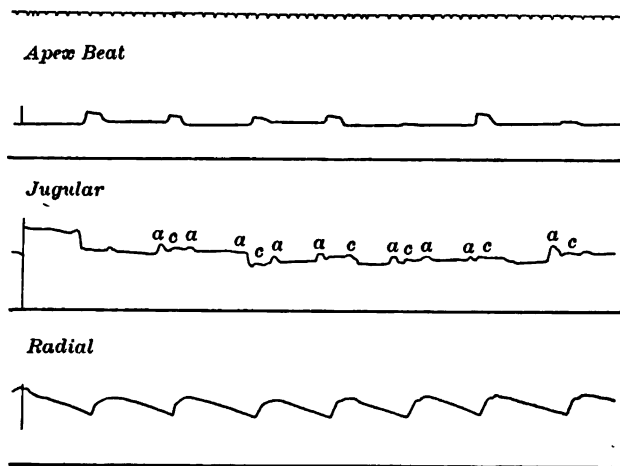


FIG. 15.—Heart-block precipitated by the administration of digitalis.

they arise from heart weakness. The heart while at rest may contract with regular force, but when increased effort is called for uniform contractions cannot be produced. The contraction is slowly accomplished and the muscle insufficiently rested by the time the next stimulus arrives. Hering has described as pulsus pseudo-alternans those cases which upon analysis prove to be the results of extrasystoles. Cases in which the smaller wave occurs too soon are extrasystolic in origin; if the diastolic period is normal, it may or may not have this origin, but if the small wave is retarded we have to deal with a true pulsus alternans. This form of arrhythmia is explained by Wenkebach as follows: With diminished contractile power, if a single normal stimulus happens to occur a trifle too early, it finds the myocardium in a still more hypodynamic condition than

\* I am indebted to Dr. A. O. J. Kelly for the opportunity of studying this case.

did the previous stimulus. As a result, the succeeding contraction will not only be smaller, but will, as has been shown by Hoffmann, be performed more rapidly. If, then, the next stimulus does not occur too late, the longer pause will permit a more perfect restoration of function, and the next wave will again be large. This, in turn, being of longer duration and its pause therefore shortened, will be once more succeeded by a smaller wave.

Clinically, *pulsus alternans* is recognized by this peculiar, regular alteration of large and small beats. Characteristic of it is the fact that once established it persists for long periods of time, being thus in marked contradistinction to the cases of extrasystole which are irregularly intermittent, as a rule, and have never been known to occur steadily and regularly for weeks. Furthermore, extrasystoles when present tend to vary their appearance during different phases of the diastolic period. The difference in the size of the two waves of a *pulsus alternans* may vary within wide limits; generally we may assume that the amount of cardiac weakness is directly proportionate to the smallness of the second wave. It also often bears a direct relation to the rapidity of the rate—the more rapid the action the greater the alteration. *Pulsus alternans* is met with in severe myocardial and valvular lesions. It is a distinctly rare condition. Wenkebach states that he has encountered but two cases. The condition is met with in the arterial hypertension of nephritis and angina pectoris, but it sometimes occurs after infections (influenza), and in such cases may disappear.

Thus far we are in possession of but little knowledge concerning stimulus production and tonicity. Gaskell has shown that the latter property may be altered by various drugs, and it has been suggested that cardiac dilatation may result from depression of this function.

**PROGNOSIS.** It is sometimes difficult to draw definite conclusions as to the prognostic importance of an arrhythmia. Of course, the age of the individual, his occupation, habits, and social condition, have to be taken into consideration. We can also obtain much valuable information from the patient's general condition, the state of the bloodvessels, arterial tension, pulse rate, etc., and especially from the effect of exertion upon these factors. We can rarely afford to prophesy on the basis of the sphygmograph alone any more than we can on the clinical thermometer and yet both of these instruments are useful adjuvants in diagnosis.

Arrhythmia of muscular origin is more serious than that due to nervous causes. As has already been pointed out, we can determine the presence of the latter by deep breathing and by the effect of the atropine test. Further, the time and cause of an arrhythmia will much modify our opinion of its seriousness. Thus, for example, extrasystoles occurring during the convalescence from infections have generally very little importance, whereas the appearance of this symptom during the fastigium is often of sinister import.

The respiratory type of irregularity is generally of trivial consequence. Extrasystoles, although often insignificant, require careful investigation, especially if occurring in middle-aged or elderly people. Perpetual arrhythmia is always serious, and the same may be said of that rare condition, pulsus alternans. Auriculoventricular heart block also is unfavorable, for although in some subjects the attacks may be precipitated by the injudicious administration of digitalis and disappear after withdrawal of the drug, and other subjects may live for a number of years despite its presence, the symptom always indicates a disturbance of muscular functionation.

### **THE PECULIARITIES OF THE SYMPTOMATOLOGY OF RHEUMATISM IN CHILDREN.<sup>1</sup>**

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THE etiology of rheumatism is still a subject for discussion, and, unlike such diseases as diphtheria and typhoid fever, its existence in any case is not susceptible of scientific proof. The claims of rheumatism to our consideration as a separate disease entity must be based, as in such diseases as bronchopneumonia, upon the specific character of the anatomical lesions, or, as in such diseases as scarlet fever, upon the specific character of the clinical picture. The peculiarities of the symptomatology of rheumatism are therefore important, not alone from their own intrinsic interest and their bearing upon the practical aspect of the disease in diagnosis and treatment, but also from the possible light which they may throw upon the unsettled question of an ultimate specific etiology.

One fact, indeed, is now generally recognized: that rheumatism is a disease that differs widely in its clinical manifestations and phenomena as we pass from earlier to later childhood, from childhood to adolescence, and again into adult life. I know of no disease common to children and adults which presents such a surprisingly different clinical picture at these two ages. I find that in beginning to demonstrate cases of rheumatism in childhood to students whose previous training has been confined to adults, its peculiarities impress them like the revelation of an entirely new disease.

In the adult, rheumatism presents itself as an acute disease characterized by inflammation in the joints, with its severe symptoms referable to the joints and with a tendency to cardiac complications

<sup>1</sup> Read by invitation at a meeting of the Philadelphia Pediatric Society, February 11, 1908.



of comparatively slight clinical significance in their immediate result. In the child, rheumatism presents itself as an acute disease characterized by inflammation in the heart or joints, or both, with its severe symptoms referable to the heart, and with a tendency to arthritic symptoms of comparatively slight clinical significance. This is the principal contrast, stated in its broadest form. In a more detailed view of rheumatism in childhood many further points of contrast, of great interest, are encountered.

As to the mode of onset of rheumatic fever, we find that in the adult the disease begins almost invariably with fever and arthritis, usually polyarthritis, characterized by pain, tenderness, redness, and swelling at the affected joints. In an analysis of 223 cases of rheumatic fever in children, I found that the mode of onset was as follows: Fever and arthritic symptoms, 88 cases; fever and cardiac symptoms, 82 cases; fever and both arthritic and cardiac symptoms, 25 cases; fever only, 18 cases; fever and sore throat, 6 cases; fever and chorea, 1 case; and unknown, 3 cases.

From this it appears that, although a little the most common mode of onset is with symptoms referable to the joints alone, an onset with symptoms referable to the heart alone is almost as common. By cardiac symptoms are meant not the evidence of insidiously developing endocarditis disclosed by the detection of a murmur, but actual symptoms of cardiac weakness, such as precordial pain, dyspnoea, and orthnopœa. It is also notable that, although the onset with arthritic symptoms alone is commoner than any other one mode of onset, yet it existed in only 40 per cent. of all the cases. The number of cases in which the disease manifested itself at the onset by the occurrence of fever only, with or without slight and vague constitutional symptoms, is of special interest in connection with the practical question of diagnosis. It shows that rheumatism in children must be placed in that class of acute infectious diseases which do not necessarily show characteristic or localizing symptoms at the onset, and in which the diagnosis must be often for several days in doubt, until such symptoms have developed. When, as so often happens, the physician is confronted with a beginning acute infectious disease, in which the physical examination and history are not illuminating, he must not forget to number rheumatic fever among his possibilities. The onset with sore throat as the only symptom accompanying the fever, in 6 cases, is also of interest. In consideration of the fact that children only complain of sore throat in a small proportion of cases in which inflammation of the pharynx or tonsils is found on physical examination, it is very possible that the number of cases in which such inflammation was acutally a symptom of onset might have been larger if proper observation could have been employed. The interest of this inflammation as an initial symptom of rheumatic fever lies in the light which it may throw upon the question of the route of invasion of the infection.

The fever of rheumatism, while showing the widest variations in different cases, both as to the degree of temperature attained and as to its duration, nevertheless presents certain features which I believe are fairly characteristic of this disease. The amount of fever varies with the severity of the case and with the localization of the infectious process, every gradation being found from the most moderate fever curve, ranging between  $99^{\circ}$  and  $100^{\circ}$ , to one reaching  $105^{\circ}$  or even  $106^{\circ}$ . Hyperpyrexia, however, is rare in children, being very much less common than in adults; in an average case in a child the fever ranges between  $101^{\circ}$  and  $103^{\circ}$  at the height of the disease. The analysis of the cases which I made two years ago revealed that the temperature is higher in the cases with cardiac symptoms than in those with arthritic symptoms only, and, in general, higher in cases of pericarditis than in cases of endocarditis. The most notable characteristic of the temperature curve in rheumatic fever is the absence of any very wide daily variation in the temperature, the variation being, in the majority of cases, about one degree, and not often over two degrees; the morning temperature is almost always the lower. There are, of course, marked exceptions to this rule to be encountered at times. Nevertheless, sudden exacerbations, remissions, or critical falls in the temperature are uncommon. The temperature usually rises rapidly, but not with extreme suddenness, and in most of the arthritic cases and the milder cardiac cases falls rapidly, but not suddenly, to the normal. The maximum is by no means always reached near the beginning of the disease, as at any time a further exacerbation may occur, in which the fever increases fairly rapidly, but again not suddenly. The course of the fever may be prolonged over a period of weeks, with frequent exacerbations, especially in the cardiac cases, the longest fevers being found in cases of pericarditis. In such cases the termination is by a much less rapid lysis than in the arthritic and milder cardiac types. The duration of fever in 223 cases was as follows:

	Average.	Extreme.
In cases with arthritic symptoms only . . . . .	4 days	1 day to 2 weeks.
In cases with endocarditis . . . . .	12 "	1 " to 12 "
In cases with pericarditis . . . . .	39 "	2 days to 12 "

In comparison with adults, the shorter duration of the fever in the articular cases, and the frequent exceedingly long duration of fever in the cardiac cases, form a very characteristic feature.

Constitutional symptoms, while sometimes present, are usually absent or slight in children. In some cases the fever of onset is accompanied by some headache and vague aching pains in the back and limbs, without pain on motion or tenderness in the joints. Such cases are frequently diagnosticated as grippe. There are almost never general symptoms referable to the nervous system. The profuse acid sweating, so commonly seen in adults, is compara-

tively uncommon in children, especially during the earlier years of childhood.

The joint symptoms of rheumatic fever in children deserve detailed mention. The first peculiarity of the disease which struck my attention in analyzing a series of cases, was the comparative infrequency of joint symptoms in children suffering from an acute infection which other evidences pointed to as being rheumatic fever. Out of 223 consecutive cases admitted to the Children's Hospital suffering from rheumatic fever, only 102 (45 per cent.) had joint symptoms. A second point is their great mildness in comparison with rheumatic fever in adults. Not only are the objective manifestations of swelling, redness, and heat comparatively infrequent, but the pain on motion is much less severe, often being so little as to cause only a slight limp, and the tenderness to pressure is often but slightly marked, or absent. Redness and swelling were present in only about 50 per cent. of the cases having joint symptoms, and in only 20 per cent. of all the cases of rheumatism in the series. The duration of the joint symptoms in children is also very brief, averaging a little less than two days.

This frequent great mildness and extremely short duration of the arthritic symptoms, combined, as they so often are, with very slight fever and no constitutional symptoms, account for the fact that rheumatism in children is so frequently overlooked. The symptoms, even when complained of by the child, are often attributed by the parent to "growing pains," and in other cases, in which the only manifestation is a slight limp in walking or complaint on using a limb, the disability is attributed to a strain.

As to the number of joints affected in children, there is wide variation. Only one joint may be affected, and the process is confined to one joint more often in children than in adults (10 per cent. of my series). Usually more than one joint is affected, but the number is in general fewer than in adults, a general polyarthritis being rare. The ankles are the joints most frequently affected, the knees being second and the wrists and hands third.

In this description of the arthritic manifestations of rheumatism I have laid stress on the general and typical peculiarities in children, but I do not wish to convey the impression that rheumatism never occurs in childhood in the same severe arthritic form as in adults. Cases are seen in which there is high fever, polyarthritis, with extreme pain on motion, tenderness, redness, and swelling, and in which there are even profuse acid sweats. Such cases are, however, not typical, and occur most often in older children. Indeed, a striking feature in the rheumatism of early life is the variation of its manifestations according to age. The younger the child, the more apt are the peculiarities mentioned above to be accentuated, arthritic manifestations being slight and cardiac manifestations prominent. The nearer adult life is approached, the more does the type of disease approach that seen in adults.

The cardiac manifestations of rheumatic fever in children are of importance, in the first place on account of their great frequency of occurrence. In my series, 91 per cent. of all cases had evidence of an organic lesion in the heart, which is a very much larger proportion than that observed in the rheumatism of adults. The commonest form is endocarditis, found in 91 per cent., pericarditis occurring in 26 per cent. It is, however, not so much this frequency of occurrence of cardiac involvement which constitutes the most important peculiarity of rheumatic fever in children, as it is the effect which acute endocarditis has upon the symptomatology of the disease. In the adult endocarditis is usually described as developing insidiously, betraying itself only by the appearance of a murmur. In children, endocarditis usually betrays itself by the occurrence of actual symptoms referable to the heart. Its occurrence may be insidious, as in the adult, but in very few of my cases did a murmur actually develop unaccompanied by cardiac symptoms. There were cases in which a murmur was found without symptoms, but in such cases it was not possible to know if acute endocarditis was actually present, or if the murmur was the relic of some previous attack. In 65 per cent. of my cases having a murmur there were actual cardiac symptoms. The symptoms themselves are the ordinary ones of cardiac weakness: dyspnoea, palpitation, and precordial pain in the milder cases, with the addition of oedema and cyanosis in the severer ones. It is not the character of these symptoms which is of importance, but their severity, obstinate duration, and danger to life. They are accompanied by fever and evidence of acute infection, and I believe the frequency of death from heart disease in children is not due to the overstraining of chronically damaged valves, but to the liability of children to acute rheumatic infection of the endocardium, causing cardiac weakness.

Another peculiarity of rheumatic fever in children lies in the occurrence of cases in which the only localization of the infection is the cardiac—the primary acute rheumatic endocarditis of childhood—cases which run a course characterized by fever and cardiac symptoms only.

The actual lesions show no important peculiarities, and are of comparatively little clinical significance. The mitral valve is very much the most frequently affected. Pericarditis in children shows no special peculiarities in symptomatology. The majority of cases go on to effusion.

One symptom of rheumatic fever, the occurrence of subcutaneous fibrous nodules, is mentioned by authorities as being more often seen in children. No case showing this symptom happened to occur in my series of 223 consecutive cases. I believe it to be rare, in Boston, at least, although its frequency may vary in different localities. It is probably more common in England.

Finally must be mentioned one of the most important peculiarities

of rheumatic fever in childhood, the liability to recurrence of the infection with varying manifestations. It is not uncommon for these recurrences completely to dominate childhood. There is no special order for the various clinical types to appear, and each attack may be mild or severe. At one time the symptoms are mainly cardiac, at other times mainly articular, at still other times a combination of both types. Any attack may be accompanied by pericarditis or followed, accompanied, or even preceded by chorea. In any attack the severity of the cardiac symptoms may lead to a fatal ending.

It is difficult to divide a disease with such varied and changing symptoms into distinct clinical types. The following division is based upon the character of the onset and the severity of the case; it must be remembered that at any time in an articular type of case cardiac symptoms may develop, and vice versa, and that even the mildest cases after recovery usually are left with a permanently damaged heart:

1. The mild arthritic type. These are cases with slight and brief fever and joint symptoms only, of a mild and brief, even fleeting, character, confined to one or few joints.

2. The severe arthritic type, occurring in older children, with a severe polyarthritis resembling the adult type.

3. Latent type. In these cases there is at the onset a period with fever as the only symptom. Later may occur cardiac or arthritic symptoms, which may be so mild as to escape notice, or which may at any time become severe.

4. Mild primary endocarditis. These cases are characterized by fever and slight dyspnoea, palpitation or precordial pain, the symptoms being of brief duration. Slight joint symptoms may develop in the course of the disease.

5. Severe primary endocarditis. These cases are characterized by fever and the whole train of the symptoms of cardiac incompetency. They usually run a prolonged and obstinate course, recovery occurring very gradually. At times death occurs from failure of the heart.

6. Mild pericarditis. In these cases precordial pain is the most prominent symptom, accompanied by fever and the other signs of cardiac weakness. They usually run a fairly long course. Effusion may or may not occur, and, a notable point, it may occur without increase in the severity of the cardiac symptoms. Cases of pericarditis almost invariably show endocardial murmurs also.

7. Severe pericarditis. In this type, the fever is high, long continued, and obstinate, and precordial pain is severe at the onset. Effusion always occurs. The symptoms of cardiac insufficiency become very marked, and their severity usually shows little relation to the amount of effusion, although at times a sudden increase in their severity occurs in parallel with a sudden increase in the extent of the effusion. Recovery is slow, and death, when it occurs, is due to cardiac weakness.

**STATISTICS OF SEVENTY CASES OF GASTROSCOPY.**

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THE superiority of inspection to deduction as a process in diagnosis requires no argument. It may be measured by the usefulness of the cystoscope. The stomach is more amenable to endoscopic methods than is the bladder, and its pathological importance is vastly greater. Curiously enough, it was the success of the Nitze-Leiter cystoscope that retarded gastroscopy. The earnest and ingenious efforts of von Mikulicz, Rosenheim, and Rewidzof in this field were ever fruitless, because they started with the radical and radically wrong principle of obtaining a view through a lateral window by an arrangement of lenses and prisms. Such an optical apparatus necessarily involves a fatal defect—a blind tip to an instrument which is passed in the dark by the sense of touch alone. Such passage of a straight rigid instrument into the stomach is not only exceedingly difficult (von Mikulicz considered it impossible in all cases, Rosenheim in many), but is dangerous.

There are several differences in anatomical conditions, not necessary to enumerate, that render the cystoscopic principle unsatisfactory here. It is sufficient to allude to the much greater size of the stomach. When one dilates the stomach he pushes its walls far away from the reach of the tube; walls which otherwise would collapse over the tube mouth, to be examined and palpated by the probe and tube. The portion of the stomach nearest the centre line of the body is the most easily examined. The collapsed stomach is relatively small, and much of it is near the middle line (Fig. 1). When one distends the stomach he pushes most of the otherwise explorable area away from the central line and thus laterally out of range. The diaphragm is rendered much less movable when the stomach is distended, and, furthermore, thus is rendered impossible the practice of a most valuable part of the technique, namely, the manipulation of the abdomen externally by an assistant, which brings into view the fundal and pyloric ends. A lens system and an inflated stomach prevent sponging away of secretions with which many lesions are covered.

The position and shape of the stomach in the living subject has been most curiously misunderstood. Fig. 2 is traced from one of the classical text-books on anatomy. Whatever may be the position and shape of the stomach in the cadaver or in the living subject after the abdomen is opened, it was certainly not in any such position in any of the seventy cases examined gastroscopically by me. My method of outlining the stomach is to find a given boundary with the extrem-

ity of the tube. The distal end of the tube is felt by the abdominal palpator, who makes a mark on the patient's skin with a skin

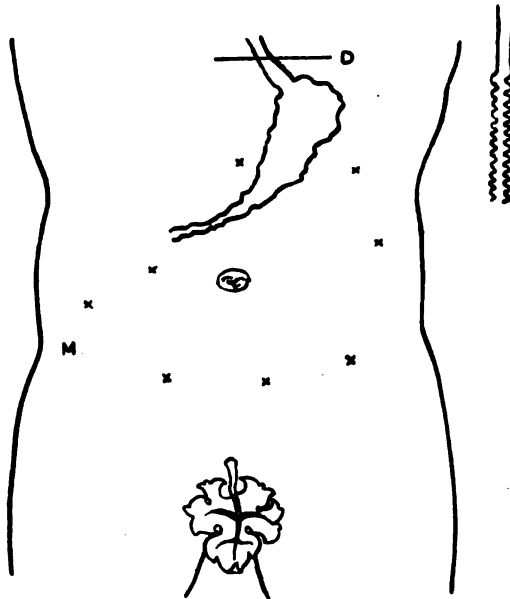


FIG. 1.—Position of the stomach in the case of Isabel A. Crosses show where the wall of the stomach was intentionally pushed by the gastroscope. The schema in the upper right-hand corner shows the other plane of the stomach.

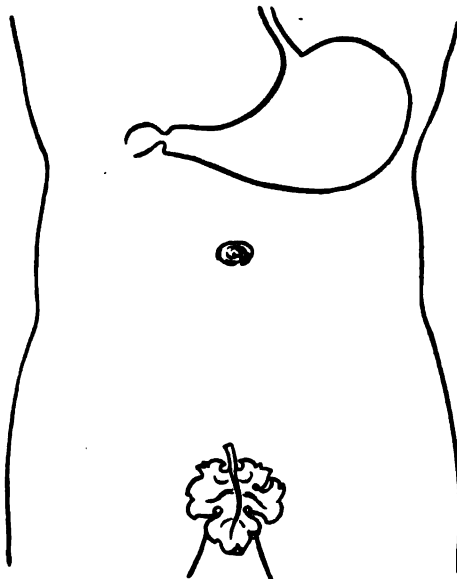


FIG. 2.—Position of the stomach as shown in a classical text-book on anatomy.

pencil. Another position on the boundary is then found and marked, and thus a series of marks dot the skin of the abdomen corresponding to the stomach outlines. An obvious source of error is the drag of the tube, which may displace the stomach. This can be avoided by a careful watch through the tube and care to make a vertical insertion for each mark.

The stomach wall can be pushed into almost any position, as shown in Fig. 1. The position of the stomach in the case of Isabel A. is shown here. It gave the impression of a loose bag dangling on the end of the gastroscope, freely movable in all directions, by either the movement of the gastroscope or the manipulations of Dr. Harold A. Miller, who was palpating the abdomen externally. The diagram at the upper right hand corner of the illustration shows schematically the other plane as it appeared to be when gastroscopically examined. Passing down the œsophagus, as soon as one passes the cardia folds and wrinkles are encountered, a slight deflection bringing either the anterior or the posterior wall into view.

The degree of motion shown in Fig. 1 is obtainable only under the relaxation of deep anesthesia. When gastroscopy is attempted, under morphine narcosis, as Mikulicz attempted it, the musculature of the diaphragm pulls upon the central tendon, so that the gastroscope is guyed rigidly like a tent pole, and if the stomach can be entered at all, only such portion can be inspected as lies in a line with the axis of the entry of the tube. When relaxed under deep anesthesia the hiatus œsophageus does not relax or enlarge so as to permit of motion; but the entire dome of the diaphragm can be moved sidewise because it is a dome. If it were a tightly stretched membrane, there would be no yield in any direction; but being arched, its "slack," as one might say, permits of a range of motion of from 10 to 15 cm., provided the central tendon is not pulled upon from all sides by the diaphragmatic musculature.

In regard to the safety of gastroscopy, my statistics show that in no instance has harm followed. Occasionally, stiffness or soreness in the neck has been noted for one or two days. There has been no other unpleasant symptom in the whole series of 70 cases, and no patient has died, from any cause whatsoever, within thirty days after the gastroscopy.

The utility of gastroscopy in the removal of foreign bodies is obvious. Its highest function, however, is as an instrument of diagnosis in the hands of the gastrologist, and of the gastroscopic assistant of the abdominal surgeon, who will assist the surgeon not only in diagnosis, but in the operating room during the operation, by working through the mouth in conjunction with the surgeon whose hand is in the abdomen.

In my gastroscopic work I have had the following positive findings in 18 patients out of the 70 examined, some patients having more than one condition:







FIG. 3.—*A*, gastroscopic view of a gastrojejunostomy opening drawn patulous by the tube mouth (patient of Dr. George L. Hays). *B*, carcinoma of the lesser curvature (patient of Dr. Joseph H. Barach, afterward surgically explored by Dr. John J. Buchanan). *C*, healed perforated ulcer (patient of Dr. John W. Boyce).

	Cases.
Chronic gastritis . . . . .	6
Gastroptosis . . . . .	3
Gastroectasia . . . . .	2
Malignant disease, cardia . . . . .	3
Malignant disease, pylorus . . . . .	3
Malignant disease, lesser curvature. (Specimen taken in two instances) . . . . .	3
Peptic ulcer . . . . .	8
Peptic ulcer cured(?) . . . . .	1
Negative results of value . . . . .	1
Foreign body removed . . . . .	1
Gastric syphilis . . . . .	1

Two cases may be cited as illustrating the possibilities of diagnosis by this method:

CASE XXV.—Isaac L., aged fifty-seven years, was referred for gastroscopy by Dr. Joseph H. Barach. For two years the patient had difficulty in swallowing. On admission he could swallow bread, but not liquids; coffee went down better than water. He had lost 13 kilograms in six months. The area of gastric tympany seemed normal, and there was no palpable mass. The patient never vomited, and the stomach tube was arrested 40 cm. from the upper teeth, so that it was impossible to examine the stomach contents. The patient was admitted to the Eye and Ear Hospital, for gastroscopy. Under the relaxation of deep general anesthesia no mass was palpable. The gastroscope was readily introduced through the cardia. His dysphagia was thus demonstrated to be due to cardiospasm, which was also visible to the eye when the patient came partly out of the anesthesia. As soon as the tube mouth reached the lesser curvature in the middle third of the stomach, I pronounced the case one of carcinoma. The appearance was characteristic and unmistakable. A mass was seen, dark gray in color, occupying a breadth equal to four rugæ. Instead of the usual pliant infolding of the normal membrane as seen through the gastroscope, the large grayish mass shown at the right in *B*, in Fig. 3, flopped in front of the tube in a way that contrasted with the size, form, and motion of the normal membrane even more than did the color.

After the examination the patient was able to swallow. He gained in weight and strength so rapidly that one of his physicians, a thoroughly competent man, disputed the diagnosis of malignancy. Pain after eating was still present, however, and the patient consented to laparotomy, which was done by Dr. John J. Buchanan. He found an inoperable carcinoma of the lesser curvature.

This was a case which, aside from cesophageal spasm, presented clinically only the functional dyspepsia which often precedes the development of the characteristic symptoms of malignancy. Yet the carcinoma, unrecognizable except by the gastroscope, had already developed beyond the hope of operative cure.

CASE XXIV.—J. G., an epileptic of rather limited intelligence, was admitted to the Western Pennsylvania Hospital, complaining of burning pain in the stomach, radiating to the right nipple. Pain

was aggravated by eating, but was present at times when the stomach was empty. The patient had lost much weight. He had vomited once only, the ejected material containing a little blood.

Gastroscopy was done under general anesthesia. The mucosa showed evidence of chronic gastritis, and was covered with thick, pasty, mucopurulent secretion. A considerable quantity of fluid pus of yellowish color poured into the gastroscope, evidently coming from the left of the cardia. Smears by Dr. W. H. Allen showed numerous bacteria, most prominent being a Gram-positive organism, probably *Streptococcus pyogenes*, and a Gram-negative diplococcus resembling *Micrococcus catarrhalis*. No opening through the mucous membrane could be found, but the pus streamed from the left into the gastroscope in a way that precluded the idea of its being a mere exudate from the mucosa. More than 100 c.c. was drawn off through the drainage canal of the gastroscope. The diagnosis, therefore, was perigastric abscess, with perforation.

More careful inquiry into the previous history showed that the patient had suffered four years previously from a severe febrile illness of two week's duration, which he reported as typhoid fever. He remembered that during this period he had suffered from a severe pain in the left hypochondrium, which compelled him to lie curled up in bed bending to the left side. His physician had told him that his "liver was enlarged." When he came to the hospital the left lobe of the liver seemed quite tender, but there was no enlargement. Whether his original abscess was subdiaphragmatic or located in the liver, I am unable to say. After gastroscopy his symptoms improved so that he refused further treatment, and soon drifted away from the city.

CASE LXIX.—Daniel B., aged sixty-two years, was admitted to the Western Pennsylvania Hospital to the service of Dr. John W. Boyce, complaining of feeling weak, and of loss of appetite, emaciation, and headache, all these symptoms appearing gradually about one year previously. There was no nausea or vomiting. The temperature was normal, the pulse 96, and the respirations 24.

After the mouth of the gastroscope passed the cardia, in the first 4 cm. of the passage, the anterior and posterior walls of the stomach opened up in normal folds ahead of the tube mouth. Below this, however, the tube mouth entered a cavity with smooth unwrinkled walls. At the bottom of this cavity was a crescentic slit-like depression looking somewhat like the primiparous os uteri (C, Fig. 3). When the mucosa was sponged clean of bubbly secretion, the slit-like depression was found to have a considerable depth, which, however, was not probed, although to have done so would have been technically easy and probably harmless. The surrounding mucosa was of pale pink color, without rugæ, and when the tube mouth was withdrawn the depression was still visible in the same position in a cavity, the wall of the stomach at this point being evidently held open by adhesions to the abdominal parietes or viscera. Fully

to appreciate the picture, it is necessary to realize that, to paraphrase, "nature abhors a cavity." The empty stomach is collapsed. When examined gastroscopically, it opens up ahead of the tube and collapses after its withdrawal, in a manner similar to that of the vagina upon the introduction and withdrawal of the vaginal speculum when used upon a patient in the dorsal position. But here was a case in which the anterior wall of the stomach was adherent, so that it was held up (dorsal decubitus); thus the posterior wall dropped away by gravity and left a cavity. The cicatrices and adhesions were such that no mucosal folds could be produced in the neighborhood of the slit. When Dr. Ogilvie tapped upon the abdomen the vibrations were seen to be beautifully transmitted in waves over the upper (anterior) wall of the stomach.

The picture was beautifully clear, and my colleagues, who saw for themselves, and I felt justified in pronouncing the lesion the cicatrix of a healed perforating gastric ulcer. Had it been an operable lesion, it could have been precisely located by holding the tube mouth against it while the abdominal surgeon cut through the stomach wall from the celiotomic wound.

CASE XX.—Margaret Z., a servant at the Western Pennsylvania Hospital. Six months before, gastrojejunostomy had been performed by Dr. George L. Hays. Complete symptomatic cure had followed. Under general anesthesia I passed the gastroscope, and readily found the anastomotic opening in the form of a slit, which, when pulled open by the instrument, showed a slightly puckered border, below which could be seen the mucosa of the jejunum (A, Fig. 3). At a point about 4 cm. from the opening was a shallow ulcer.

Apart from the ease of examination, this case is interesting in showing the existence of an ulcer, in spite of perfect symptomatic cure. Postoperative study of ulcer cases will perhaps show interesting results. Dr. Braasch, of the Mayo clinic, wrote me (September, 1907) that he has observed a Murphy button in situ after operation. Dr. W. L. Rodman, with my assistance, examined gastroscopically a gastrojejunostomy wound two weeks after operation, and saw the opening and the non-absorbable sutures in situ.

Gastrology is perhaps the most satisfactory as to diagnosis of all departments of internal medicine. But this satisfaction is relative, not absolute. Psychic affections sometimes so closely simulate ulcer (even to the apparent vomiting of blood) that the distinction is only made by what seems an intuition that belongs rather to the art than the science of medicine. Carcinoma of the stomach is rarely recognized in time for curative operation. Syphilis of the stomach is well known pathologically, but in so complete a work as *Nothnagel's System*, one leaf seems enough to cover our knowledge of its clinical history. There is, then, in this department alone room for direct inspection to work as great a revolution as did physical methods in thoracic disease.

## MYELOGENOUS LEUKEMIA AND ITS TREATMENT WITH X-RAYS.

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IN the last two years there have been 4 cases of myelogenous leukemia observed at the Cooper Medical Clinic, and to these I am adding one seen in private practice. In this same period at the clinic we have seen 1 case of Hodgkin's disease, 1 of Banti's disease, no cases of lymphatic leukemia, no cases of pernicious anemia, and 1 case of anemia with enlarged spleen of doubtful nature. Of some 700 purely medical cases seen yearly at the above clinic, there are 2 or 3 of myelogenous leukemia. As to the etiology, there is nothing positive to say. Two of the patients resided for many years in the malarial districts of California, and still denied ever having had malaria. In only one case was there a history of this infection. Nor were there any other features to which etiological importance could be attached. A history of syphilis was not obtained in any of our patients. All were men varying in age from forty to sixty-two years. Their antecedents and offspring had not suffered from any similar disease. On purely clinical grounds a certain incomplete resemblance to malignant disease was thus seen; this has been commented upon by other observers. The resemblance is further borne out by the course of the disease, its reaction to the x-rays, and its occasional improvement by intercurrent infection.

Opinions are divided as to the pathology of the leukemias and Hodgkin's disease. Some regard the processes as essentially hyperplasia, the increased number of leukocytes in the blood, due, in the case of lymphatic leukemia, to the passive washing out of lymphocytes into the blood current, and in myelogenous leukemia to the active migration of various forms of leukocytes following chemotactic influence. More recently these diseases have been regarded as malignant. Atypical growths of cells and a tendency to invade the capsules of the lymph glands and adjacent tissues are the indications of this malignant nature. According to Banti,<sup>1</sup> all leukemias and Hodgkin's disease are really neoplastic. The anatomical changes in the bone marrow, lymph glands, and spleen, where large groups of new cells invade neighboring tissues, are those of sarcomatosis. The walls of the bloodvessels, especially the veins, and even the surrounding bone, are invaded, and the changes in the blood are simply due to the tumor cells gaining entrance to the circulation. If such invaded vessels be thrombosed, the number of leukocytes will drop. In pseudoleukemia such sarcomatous

cells have not entered the circulation. When they do, the case becomes clinically one of lymphatic leukemia. Banti regards as true metastases the enormous growths of myeloid or lymphatic tissue in other viscera. Myelogenous leukemia, according to this view, is a systemic myeloid sarcomatosis of the blood and lymph-forming apparatus, while lymphatic leukemia is a systemic lymphadenoid sarcomatosis of these organs. A similar view of malignancy concerning Hodgkin's disease, largely based on anatomical findings, has been expressed by Walter Gibbons.<sup>2</sup>

Clinically, leukemia corresponds closely to malignant neoplastic conditions, and the following clinical factors support the view that it is really a malignant disease: Its onset is insidious. It is practically always fatal. The cachexia of leukemia occurs in the practical absence of fever. It is occasionally benefited by intercurrent affections, a feature true even of such an eminently malignant disease as cancer of the breast. It is usually favorably influenced by the x-rays. Objections based on the rare occurrence of spontaneous recovery in the disease are not very forceful, since similar instances of spontaneous recovery have been observed in undoubted cases of malignancy (Czerny),<sup>3</sup> as, for instance, after incomplete operation, or after intercurrent infection in cancer of the breast. That, in a few recorded cases, a marked hereditary tendency has been noted in leukemia does not harmonize with the usual picture of malignancy. As for the acute leukemias—aside from the blood findings, they do not resemble closely the chronic forms.

Pathologically, the large accumulations of new cells found in the tissues in myelogenous and lymphatic leukemia, pseudoleukemia (Hodgkin's), and chloroma have been differently interpreted. Some pathologists have regarded the picture as essentially that of hyperplasia (Lazarus,<sup>4</sup> Pinkus<sup>5</sup>) occurring in the bone-marrow, lymph glands, and spleen. Others—and I have already cited Banti—believe that the new growths are malignant. In favor of the latter view in myelogenous leukemia is the finding in many organs (lung and liver, for instance) of masses of cells identical with those of bone-marrow, foreign to the particular organs involved, apparently metastases. Growth of this new tissue may also be by direct extension.

In chloroma—green cancer of d'Aran—in which the blood is identical with lymphatic leukemia, this invasive character is particularly marked. Collections of new cells of a greenish color form in and between the bones, especially of the skull and face. By compression blindness, deafness, and various paralyses result. These greenish tumors also occur scattered through the different organs. Stengel<sup>6</sup> calls the disease sarcomatous.

<sup>2</sup> AMER. JOUR. MED. SCI., Nov. 1906.

<sup>4</sup> Nothnagel's System, 1901.

<sup>6</sup> Text-book of Pathology, 1903.

<sup>3</sup> Zeitschrift f. Krebsforschung, 1907.

<sup>5</sup> Ibid.

In lymphatic leukemia the question, too, is how to interpret the new formations. Are they lymphomas of hyperplasia, or are they malignant and sarcomatous?

In another class of cases, however, the combination of leukemia and anemia, called by Leube leukanemia, the resemblance to an acute infection or acute toxemia of rapid onset is striking. Such a case, in which the blood resembled that of a severe leukemia, ending in three and a half months with recovery, was recently described by Teeter<sup>7</sup>. Emerson,<sup>8</sup> in describing 3 cases of acute leukemia, points out the resemblance clinically to an acute infection of the bone-marrow.

**SYMPTOMS.** These are insidious. One man of our series kept at work seven months after first noticing any disturbance. The first symptoms noted by the patients were dull pains in the left abdomen, and those of anemia, such as weakness, dyspnoea, and pallor. A tumor in the left abdomen was noticed by two of the men. More particularly for the relief of the pain did they go to the physician; this was not severe, so that the first visit was postponed for weeks or months. In 1 case there was also substernal pain. The anemic symptoms were also insidious in onset and had no special characters. In 2 cases there was vomiting and in 2 cases epistaxis. Ringing in the ears and dizziness were the only nervous symptoms noted, and these could also be attributed to anemia. In 3 cases the appetite remained good. In the others it was lessened. The bowels were regular. A loss of weight was usually noted, although it was not excessive. In 1 case this amounted to 19 pounds in two years. One patient was still well nourished. With the progress of the disease the emaciation increased. The skin looked pale, in 1 case it was jaundiced. Arsenical pigmentation and evidence of slight *x-ray* dermatitis about the splenic region were observed, due to treatment. Slight oedema at the ankles was found in all cases. The pulse, often rapid, was not distinctive. The temperature was elevated at some time in all the cases.

The lungs were found uninvolved in 3 cases. In the fourth case an old tuberculous lesion was overlooked. The fifth case has now a lesion of the right apex, doubtlessly tuberculous. Enlargement of the cardiac dulness transversely occurred in 4 cases. The largest heart extended from the right sternal border to 4 cm. to the left of the left mammary line. A faint systolic murmur was noted occasionally at the apex or base, but in no case was a diagnosis of endocarditis made. Enlargement of hepatic dulness was present in all cases, though the edge of the organ was not always felt. In one case the vertical measurement in the right mammary line was 22 cm. When the liver edge was felt, it was found firm, smooth, and rather

<sup>7</sup> Jour. Amer. Med. Assoc., February 16, 1907.

<sup>8</sup> Johns Hopkins Hosp. Bull., March, 1907.



rounded. The spleen was enlarged in all cases. In 3 it was enormous, filling out nearly the entire left side of the abdomen; and in these and in a fourth case the splenic tumor was easily seen on inspection of the abdomen. The largest splenic dulness measured 32 x 30 cm., reaching to 6 cm. below the umbilicus and 2.5 cm. to the right of the median line. The organ felt firm, smooth, its edge somewhat rounded and notched more than normally. It was not painful to palpation. The size of the spleen in a general way varied directly with the condition of the patient and with the number of leukocytes, diminishing in size as the patient convalesced and as the leukocytes diminished. Comparing different patients, however, no such parallelism occurred; for instance, in Case I, at a time when there were 632,000 leukocytes per c.mm., the spleen reached at expiration only 4 cm. below the costal margin; while in Case V, with 48,000 leukocytes, the organ extended 6 cm. below the umbilicus. Both of these cases were seen about six months after the first symptoms had appeared. There was slight general enlargement of the lymph glands in Case IV, possibly due to the tuberculous infection subsequently found. In Case III the lymph glands were somewhat enlarged, but not tender. The nervous system and genitalia were negative. The urine in 3 cases showed at first only a trace of albumin, with hyaline and granular casts in 2 cases.

*Blood.* In this series of cases the average number of leukocytes when first seen was 312,000; that of the red cells was 2,860,000. The relation of white to red cells was that of 1 to 9. The average hemoglobin content was 50 per cent. When first seen the myelocytes constituted from 30 to 64 per cent. of all the leukocytes. Under the x-rays their numbers were both actually and relatively reduced. Through the influence of an acute miliary tuberculosis in one case they disappeared entirely. The leukocytes in this case dropped from 300,000 to 6000 in five weeks.

This brings up the interesting point of the influence of complicating infections upon leukemia, a subject extensively considered by Dock.<sup>9</sup> From the literature and from his cases, it is shown that, under the influence of complicating infections in leukemic patients, there is a disposition for the leukemic characters of the blood to disappear more or less completely, the spleen, liver, and lymph glands often growing smaller. In the majority of cases the leukocytes are diminished. In about half the cases the number is reduced to normal or less than normal. These conditions hold true for acute infections, in which the number of leukocytes may rapidly diminish within such a short period even as three to ten days. In one of our cases the eosinophilia were absent in several examinations, a feature also noted by Simon. Joachim<sup>10</sup> has recently described 2 cases of what he calls

<sup>9</sup> AMER. JOUR. MED. SCI., April, 1904.

<sup>10</sup> Deutsch. Archiv f. klin. Med., lxxxviii.

"mast-cell leukemia." These mast cells constituted over 50 per cent. of the leukocytes present. It is a variety of myeloma with a prognosis less favorable than the ordinary form. The blood findings in our 5 cases are epitomized in Chart I.

CHART I.—THE BLOOD IN FIVE CASES.

Date.	Red cells.	Hemoglobin.	Leukocytes.	Small mononuclears.	Large mononuclears.	Polynuclears.	Eosinophiles.	Myelocytes.	Basophiles.	Nucleated reds to 500 leukocytes.	Remarks.
Case I.											
Aug. 23, 1905.	2,000,000	30-35	632,000								
Jan. 23, 1906.	3,120,000	60.0	3,400	20.0	10.0	66.7	0.0	3.3	0.0	0.0	Patient doing well.
Apr. 9, 1907.	3,464,000	60.0	85,280	4.6	2.8	69.7	1.8	21.0	0.0	2.0	
Case II.											
Mar. 24, 1905.	4,000,000	67.0	172,000	13.0	10.0	37.0	2.0	31.0	3.0	0.0	Death Sept., 1906
Case III.											
May. 31, 1905.	2,500,000	42.0	570,000	3.0	1.0	30.0	2.0	64.0			
Aug. 21, 1905.	3,650,000	70.0	83,600	4.0	7.5	63.1	1.0	23.9	0.5	7.0	Death Oct. 29, '05
Case IV.											
Nov. 22, 1905.	2,750,000	53.0	160,000	2.5	0.5	40.0	1.5	55.0	1.0	7.0	Miliary tuberculosis
Dec. 26, 1905.	2,220,000	38.0	3,600	4.0	8.0	88.0	0.0	0.0	0.0		Death Jan. 1, '06
Case V.											
Mar. 11, 1907.	3,050,000	55.0	72,000	5.0	3.3	51.7	2.0	30.4	7.6	4.0	Left the wards
Apr. 6, 1907.	3,950,000	60.0	63,600	0.6	1.9	53.3	6.7	37.0	0.6	2 normoblasts.	

**DIAGNOSIS.** In these cases with a typical blood picture and enlarged spleen the diagnosis was easy. Mixed forms, however, do occur, such as those seemingly combined with pernicious anemia. In lymphatic leukemia the diagnosis is evident by the increase of lymphocytes; myelocytes are not found. In cases of so-called aplastic leukemia, in which the clinical picture of leukemia is present, but with no increase of leukocytes, the diagnosis is based upon the changed blood formula. In an anomalous case studied by Ewald,<sup>11</sup> lasting seven weeks, autopsy findings were identical with myelogenous leukemia, and still the blood gave no sign of it during life.

**COURSE AND PROGNOSIS.** The prognosis is bad. The disease, in most cases, progresses in spite of treatment and terminal infectious or terminal hemorrhages are likely. Still, with the palliative action of the x-rays the prognosis would seem to be better than formerly. This bad prognosis is exemplified in our 5 cases. In Case III death occurred with anasarca and subdural hemorrhage two and

<sup>11</sup> Berliner klin. Woch., xlii, Nr. 26.

one-half years after the onset of the illness. In Case IV death resulted from miliary tuberculosis nine months after the first symptoms of leukemia. In Case II death ensued two and one-half years after the onset of the first symptoms. Case V has been seen only recently. The patient has been sick for six months, and has at present a catarrh of the right apex, no doubt tuberculous. Case I is remarkable, and will be spoken of especially under treatment. With occasional applications of the  $x$ -rays for eight months, at the end of a year he had practically recovered. It is now over two years since his symptoms were first noted, and in spite of the fact that he was sixty-two years of age, had a distinctly dilated heart and a good trace of albumin in his urine, with 632,000 leukocytes per c.mm., and with the hemoglobin at 30 to 35 per cent., he is now practically well, able to handle his business interests, and is otherwise strong. The blood picture, however, is far from normal.

**TREATMENT.** As in other severe chronic conditions, it is imperative that the patient be well fed and receive considerable rest. Our clinic patients were put to bed. They received the regular ward diet, with laxatives as required. Under this careful *regime*, with applications of  $x$ -rays, they were able to leave the ward, except in one instance, in a few weeks and return to light work. They then received  $x$ -ray applications once or twice weekly as ambulatory patients. Eventually, as their conditions grew worse, they returned to the ward, with the results previously given. Owing to gastrointestinal irritation, arsenic, either as Fowler's solution or Asiatic pill, was found unsatisfactory. Hypodermic use of arsenic was not tried. By far the most satisfactory results were obtained by giving  $x$ -rays in small and repeated doses. Except toward the approach of death, the patients grew stronger and the spleen and liver were reduced in size. The leukocytes, especially the myelocytes, were quantitatively reduced. The red cells and the hemoglobin were more difficult to influence. The latter could not be raised to normal; and, even in our most favorable cases, myelocytes were still found.

The method of application of the  $x$ -rays can be best illustrated by following Case I. Applications were made three times weekly for three months, then every five days for two months, and as the blood picture improved and the patient improved the treatment was given at longer intervals. The current was obtained from a coil; a medium high or medium tube was generally used, occasionally a medium soft; the distance of the tube from the body was 25 to 30 cm; time of exposure, seven to fifteen minutes; amperage, 7 to 10 with the higher tubes; voltage, 10 to 120. Interruptions were made with a Wehnault or mechanical interrupter (2600 to 3000). The regions exposed were the splenic, anteriorly and posteriorly, the dorsal, the two thighs, the epigastric, and the sternal. Dermatitis was carefully avoided. The  $x$ -ray applications were

started three weeks after the patient was first seen. During these three weeks while taking arsenic and iron, he had grown appreciably worse, but with the beginning of the *x*-ray treatment the improvement began and continued as long as the *x*-rays were given. This improvement was felt by the patient himself, was found on physical examination, and was particularly striking in the changed blood picture. At the beginning of treatment the blood was as follows: red cells, 2,000,000; white cells, 632,000; hemoglobin, 30 to 35 per cent. Three and a half months afterward the reds were 3,784,000; whites, 8400; hemoglobin, 50 per cent. In September, 1906, five months after the cessation of *x*-ray applications, the reds were 4,000,000; whites, 10,000; hemoglobin, 70 per cent. A palliative though far less successful effect was shown in three other patients. The number of treatments given monthly with the changed blood picture are tabulated in Chart II. Case IV was complicated by miliary tuberculosis, so that the results were obscured; and in Case V also we believe pulmonary tuberculosis to exist. In Case I the result, as stated, was striking. It was not necessary to place this patient in bed. He lived at home and came to the Lane Hospital for his *x*-ray applications. Possibly the better result in this case was due partly to the fact that the patient was better able to care for himself, the other 4 being clinic and dispensary patients.<sup>12</sup>

The palliative action of the *x*-rays in leukemias and pseudoleukemias is now generally conceded. Indicating the profession's interest, Shirmer<sup>13</sup> was able to collect 109 articles on the subject published in two years. We have had no experience with the *x*-rays in lymphatic leukemia, but in 1 case of Hodgkin's disease, of four years' duration, the general condition of the patient has been much improved and the affected lymph glands made considerably smaller by the *x*-rays. Most of the good results, however, have occurred in cases of myelogenous leukemia. Cheney<sup>14</sup> has reported one such case, seen at the Lane Hospital. It must be understood distinctly, however, that in the leukemic conditions the *x*-rays are not curative. They are at most palliative; relapses occur under this as under other methods of treatment, but for several months—over twelve in one of our cases—the patient may be free of symptoms. In a small number of cases, approximately 10 per cent., the treatment seems valueless, or even harmful. The action on the leukocytes may be rapid. After a preliminary rise within a few days or in a few hours there may be a diminution of many thousands. The mononuclears are particularly affected. The red cells and hemoglobin may or may not be increased, but a more definite achievement is the improvement of the patient, as shown by increased appetite, increased

<sup>12</sup> I acknowledge with thanks the kindness of Dr. Oliver, of the Cooper Pathological Department, and of Dr. Lehman, of the Cooper Dermatological Department, in furnishing some of these data.

<sup>13</sup> Central. f. d. Grenz. d. Med. u. Chir., ix, 15.

<sup>14</sup> Medical News, 1904

CHART II.—RECORDS OF BLOOD COUNTS WHILE PATIENTS WERE UNDER TREATMENT.

Date.	X-ray applications during the month.	Red cells.	White cells.	Hemoglobin.	Remarks.
Case I.					Per ct.
Aug. 23, 1905.	3	2,000,000	632,000	30-35	
Aug. 29, 1905.		2,240,000	528,800	40	
Sept. 6, 1905.	13	2,500,000	255,200	40	
Sept. 16, 1905.		2,360,000	245,600	38	
Oct. 4, 1905.	13	3,000,800	380,800	50	
Oct. 24, 1905.		3,160,000	133,600	52	
Nov. 2, 1905.	6	3,550,000	62,400	55	
Nov. 28, 1905.		3,620,000	13,200	60	
Dec. 16, 1905.	6	3,784,000	8,400	60	
Jan. 4, 1906.	6	3,968,000	16,800		Laryngitis of 10 days' duration.
Jan. 28, 1906.		3,120,000	3,400	60	
Feb. 14, 1906.	4	3,440,000	3,000	60	
Mar. 10, 1906.	4	2,820,000	4,600	60	
Apr. 3, 1906.	4	2,400,000	3,600	50	Discontinued x-rays after earthquake of 1906.
Sept. 18, 1906.		4,000,000	10,000	70	
Apr. 9, 1907.		3,464,000	85,280	60	
May 10, 1907.	2	3,536,000	109,100	70	
June 14, 1907.	4	4,100,000	104,800	67	
July 24, 1907.	4	4,100,000	165,000	67	
Case II.					
Apr. 7, 1905.	4	3,960,000	146,000	67	Has been receiving x-rays elsewhere; now ambulatory.
Apr. 28, 1905.		4,000,000	100,000	75	
May 3, 1905.	13	4,000,000	97,000	75	
May 24, 1905.		3,750,000	116,000	72	
June 2, 1905.	13	4,000,000	140,000	78	
June 30, 1905.		3,600,000	115,000	74	
July 11, 1905.	13	3,900,000	70,400	76	
July 28, 1905.		4,000,000	54,000	80	
Aug. 16, 1905.	13	4,050,000	41,600	76	
Aug. 24, 1905.		4,000,000	80,000	80	
Sept. 1, 1905.	9	4,250,000	40,000	80	
Sept. 27, 1905.		4,650,000	60,000	82	
Oct. 5, 1905.	13	4,650,000	79,000	80	
Oct. 25, 1905.		4,650,000	56,000	80	
Nov. 9, 1905.	13	3,500,000	54,000	76	Entered Lane Hospital Nov. 30.
Nov. 22, 1905.		3,900,000	64,000	75	Left hospital Dec. 14.
Dec. 7, 1905.	2	3,730,000	40,000	74	
Dec. 27, 1905.		4,000,000	70,400	80	
Jan. 10, 1906.	4	3,500,000	80,000	68	Ambulatory; reentered Lane Hospital Jan. 19.
Jan. 31, 1906.		3,250,000	90,000	68	Left hospital Feb. 5, reentered Feb. 15.
Feb. 12, 1906.	10	3,500,000	104,000	67	Left hospital April 16.
Feb. 20, 1906.		3,300,000	112,000	65	X-ray treatment then discontinued.
Mar. 5, 1906.	13	3,500,000	160,000	63	Death in September.
Mar. 14, 1906.		3,000,000	160,000	54	
Apr. 2, 1906.	7	3,000,000	120,000	55	
Apr. 10, 1906.		3,350,000	78,000	64	
Case III.					
May 15, 1905.	8	3,150,000	456,000		
May 31, 1905.		2,250,000	510,000	42	
June 12, 1905.	13	2,600,000	460,800	50	Entered Lane Hospital June 28, 1905
June 30, 1905.		2,100,000	563,000	42	
July 11, 1905.	19	2,500,000	540,000	45	
July 19, 1905.		3,000,000	320,000	54	
July 26, 1905.		3,250,000	180,000	60	
Aug. 2, 1905.	15	3,350,000	187,600	62	Left hospital Aug. 16.
Aug. 16, 1905.		3,650,000	104,000	70	
Aug. 30, 1905.		3,500,000	80,000	70	
Sept. 5, 1905.	13	3,650,000	70,000	70	Ambulatory.
Sept. 27, 1905.		3,350,000	136,000	64	
Oct. 12, 1905.	11	2,800,000	260,000	50	Reentered hospital Oct. 16; death, Oct. 28, '05.
Oct. 25, 1905.		2,600,000	208,000	50	
Case IV.					
Nov. 14, 1905.	3	2,750,000	300,000	50	Entered hospital Nov. 21, 1905.
Nov. 22, 1905.		2,750,000	160,000	53	
Nov. 29, 1905.		3,950,000	160,000	77	
Dec. 7, 1905.	9	2,750,000	40,000	52	Death, Jan. 1, 1906; miliary tuberculosis.
Dec. 21, 1905.		1,850,000	6,000	36	
Dec. 28, 1905.		2,220,000	3,600	38	
Case V.					
Mar. 11, 1907.	4	3,050,000	72,000	55	Entered Lane Hospital, March 19; x-rays given first, March 20.
Mar. 22, 1907.		3,100,000	64,000	55	
Mar. 30, 1907.		3,450,000	45,500	60	
Apr. 6, 1907.	3	3,900,000	63,600	60	Left hospital, April 6.

strength and weight, and in women by the reappearance of menstruation. The spleen and liver usually grow smaller.

As to the mode of action of the  $x$ -rays, we know that a leukolytic body or bodies develop under treatment. Helber and Linser<sup>15</sup> have shown that serum from an animal treated with  $x$ -rays, when injected into another animal, causes a leukopenia. Control serum caused a leukocytosis. The extract of the still living, though extirpated, spleen, which organ had been exposed for several hours to the  $x$ -rays, caused a reduction of leukocytes upon being injected into the normal animals. The extract of a control spleen not exposed to the  $x$ -rays produced a leukocytosis (Milchner and Wolf<sup>16</sup>). The most convincing work along this line has been done in this country by Capps and Smith.<sup>17</sup> It was proved by them that the serum of leukemic patients improving under  $x$ -ray treatment causes a leukopenia when injected into animals; added to a hanging drop of leukocytes from another individual, a disintegration of cells, especially the mononuclears, occurs. They also injected such serum into another leukemic patient not under  $x$ -ray treatment and succeeded in demonstrating a rapid and decided drop of leukocytes in the injected patient. With repeated injections, however, a partial immunity to the injected serum was established. Whether this leukolytic substance or substances prevents the excessive formation of leukocytes in the blood and lymph-forming organs, or dissolves the leukocytes after they have been formed, is not known. Nor have the studies of metabolism, especially concerning the uric acid output of patients or animals treated with  $x$ -rays, helped to solve the problem. We can, however, say that it has been demonstrated that the blood of leukemic patients and of animals treated by  $x$ -rays contains a body or bodies capable of dissolving the leukocytes.

CONCLUSIONS. 1. At present it is best to consider myelogenous leukemia a malignant neoplastic disease.

2. The  $x$ -rays are effective in treatment as a palliative measure.

3. The action of the  $x$ -rays is associated with the production in the patient of a leukolytic body or bodies.

<sup>15</sup> Deut. Archiv f. klin. Med., lxxxiii, 1905.

<sup>16</sup> Berliner klin. Woch., xliii, Nr. 23.

<sup>17</sup> Jour. Exp. Med., January, 1907.

**PYELONEPHRITIS COMPLICATING THE PUERPERIUM.**

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WHEN the upper urinary tract becomes obstructed and the contents of the accidental cyst thus formed become infected, four symptoms will be met with together or in succession—pain (localized in the lumbar region on the side of the lesion, or on both sides if the lesions are bilateral), vesical disturbances, a rise in temperature, and pyuria. Before considering this symptomatology in detail, I wish rapidly to sketch the usual manner in which the various pyelonephritides make themselves manifest after labor.

The commencement of the renal process may often be insidious and early. A patient does not do well during the first two days after delivery, each evening showing a slight rise in temperature, so that the physician immediately begins to suspect an infection of the uterus. Pain very infrequently indicates the renal lesion, and may not develop at the beginning of the process, so that the patient does not complain of the renal region. In other cases, the commencement of the disease may be very sudden and occur late in the puerperium. There will be a severe chill and a sudden rise in temperature, accompanied by marked pain. From recorded cases I think one may assume that the descending pyelonephritides are of rather slow development, while the ascending forms appear very shortly after infection of the lower urinary tract, as in the following case:

The patient, aged twenty-four years, had always been genitally well and had never suffered from any symptoms which could be related to the bladder or urethra. Married thirteen months ago, she had become pregnant. During labor, which was rather slow, the nurse was obliged to pass the catheter three times on account of vesical inertia. The family physician delivered the patient with low forceps after she had been twenty-six hours in labor. The child weighed  $8\frac{1}{2}$  pounds. After delivery it was necessary to resort to the catheter every six hours for the next twenty-four hours on account of the persisting vesical inertia. On the fourth day the lochia possessed a strong odor and was lessened in amount; the evening temperature showed a rise of  $1.5^{\circ}$ , so that intra-uterine irrigations were resorted to morning and evening. The evening temperature continued to increase, while in the morning the temperature never reached normal, and, as the lochia continued rather foetid, the physician was inclined to diagnosticate a mild form of uterine sepsis, and I was asked to see the patient in consultation.

I saw her on the sixth day of the puerperium, and made the following notes: She had been passing her urine spontaneously, for the past three days. It was found cloudy, and the cloudiness appeared universally distributed throughout the test-tube. Upon palpation of the abdomen, deep-seated pain could be elicited in the right lumbar region, but the pain was not spontaneous unless the patient moved quickly in bed. The left lumbar region appeared in every way normal. On account of these functional symptoms, I was inclined to eliminate the diagnosis of uterine infection, and made one of right-sided pyelonephritis. There was no evidence of cystitis, although the bladder presented some tenderness on suprapubic palpation, but there was no pain on micturition.

On the eighth day the urine was passed in much larger amount, but was still turbid, and when allowed to remain in the test-tube the sediment composed about one-fourth of its bulk. This sediment was found to contain nothing but pus and large numbers of bacteria, which, by bacteriological examination, proved to be colon bacilli.

The treatment consisted in a milk diet, large quantities of water, and the administration of 0.5 gram (7.5 grains) each of salol and urotropin, three times daily. Four weeks after my first visit the urine upon microscopic examination was found perfectly normal and the patient had returned to her former health.

No matter how the renal affection may make its appearance, the following are the characters of each of its symptoms: The pain is seated in the lumbar region, topographically limited above by the border of the ribs, inwardly by a line drawn through the umbilicus, while it often happens that it radiates downward, following the direction of the ureter, as in nephritic colic. Laterally there is no fixed limit; the painful area consequently corresponds to what is ordinarily termed the flank. The pain is persistent in most cases, deep-seated, and paroxysmic, and varies much in intensity. It is increased by movements on the part of the patient, and especially when bimanual palpation is practised, just as in the case of peritonitis or appendicitis. It does not seem to be increased by micturition, but any effort producing contraction of the abdominal muscles makes it appear. As to the time of its appearance during the evolution of the affection, nothing absolute can be said; but it usually begins with the renal process and ends when the latter is recovered from, while its diminution is notably evident when the ureter on the diseased side is allowing the passage of the pus, while, at the same time, and from this very reason, the temperature shows a tendency to subside.

The bladder disturbances may be considered under two heads. First, one may be dealing with a cystitis present before the development of the renal affection, or concomitant with it; under these circumstances there are all the classical symptoms of inflammation of the bladder, from which follows an ascending involvement of the



ureter and renal pelvis. In the second class of cases one is dealing with vesical disturbances without infection of the bladder, and this is what is more ordinarily observed. Therefore there are no real pains on micturition, excepting when a ureteritis has apparently been the factor in the production of the cystitis; there is no tenesmus and only a slight painful sensation when the organ is pressed upon suprapubically, which, for that matter, may be the result of extension of the pain along the ureter. This slight amount of participation, on the part of the bladder, in the pain resulting from pyelonephritis may be placed under the head of reflex cystalgia, which is symptomatic of some lesion involving some part of the genito-urinary tract. It should be recalled that the bladder is not easily inoculated by a dirty catheter, as I shall endeavor to point out later.

The third symptom is fever. This usually occurs as an evening rise, the morning temperature never falling to the normal. During the entire duration of the renal affection a rise in temperature need not of necessity be constant, because oftentimes it occurs in paroxysms dissociating the painful phenomena to which it may succeed, and, sometimes indicating their temporary or final disappearance. The chart will show from 39° to 40° C., or even more, because infection of the renal pelvis, under the influence of tension, will give rise to more fever than any other infectious lesion of the urinary apparatus. Although the temperature may remain high, the general condition of the patient is usually relatively good, and, although the tongue is coated, it remains moist and rose-colored, and not that bright-red tongue accompanied with marked dryness that is present in severe forms of infection. The pulse is rapid, and, although sometimes of high tension, it never becomes filiform. The mildness of these symptoms may be attributed to the fact that the intact kidney suffices for the elimination of the toxins. If delirium supervenes, it is rarely serious and is of very short duration.

Polyuria and pyuria are present. The urine is cloudy and in amount averages from two to two and one-half quarts in twenty-four hours. It is a pale yellow in color, cloudy, and more or less milky, while occasionally it may contain sand. The quantity of urine, which at first may appear diminished on account of the poor functioning of one of the kidneys, is in reality normal and not infrequently increased. This fact is explained by the law of compensation of symmetrical organs, and the well-known experiments of Strauss and Germont have proved beyond a doubt that the healthy kidney increases its functions and secretes a greater quantity of urine. Usually a small amount of albumin is present, this varying from 1 to 2 grams, while microscopically granular leukocytes in fairly large numbers accompanied by numerous epithelial cells, hyaline casts, and pus cells are to be seen. Bacteria are ordinarily present.

In pregnancy there are two undoubted pathogenic factors: (1) The uterus, according to the position that it assumes during the

second stage of its evolution, and as this tends more frequently to the right, it compresses the right ureter, while, should the organ lie toward the left, the left ureter is compressed, a condition of affairs relatively rare. The ureter becomes compressed by the uterus at the point where it passes over the bony projection of the superior strait at the level of the sacro-iliac symphysis. This pressure occurs more particularly during the last two months of pregnancy, and although certain German writers have considered that the child's head when engaging in the small pelvis compresses the ureters, I do not think that this is ordinarily the case.

When one ureter has become compressed, stagnation and retention in the renal pelvis result, placing the kidney in danger of infection, the chances of which are all the greater, on account of the special condition of auto-intoxication occurring in the pregnant female. It would be quite useless to waste time to demonstrate that a pregnancy, no matter how fortunate, lessens those natural resources necessary for combating the agents of infection. This agent, in the cases I am now considering, is usually the colon bacillus, either alone or associated with other organisms, whose preponderance over the former may sometimes be considerable.

We may consider whether in the puerperium, the three causes of pyelonephritis, the microbe, the soil, and the etiological cause, are active. As to the microbe, the researches of Reblaud, Weiss, and Weill show that the colon bacillus is particularly prevalent in puerperal pyelonephritides, and this has been found to obtain in my own cases. The organism may reach the kidney either by descending infection or by ascending infection. In those cases in which no digital examination or instrumental interference has been resorted to on the lower urinary tracts, in which there is neither a former or coexisting cystitis or urethritis, it is only possible to admit that the starting point of the renal infection is the intestinal mucosa.

To make this assertion more evident, I would record the following case: The patient, a primipara, aged twenty-seven years, was seen in consultation, the following notes being furnished by her family physician: The labor lasted fourteen hours, and was in every way normal. The child was being breast fed. Twelve days after labor I was asked to see the patient. For several days she had been complaining of pain in the right lumbar region, accompanied by marked constipation. The temperature was 39.2° C.; pulse, 115. Her face had an anxious look, one of infection, and the tongue was heavily coated. Palpation from the lumbar region on the right side almost to the iliac fossa gave rise to considerable pain, and, on account of the muscular rigidity, the examination was rendered difficult. There were no bladder symptoms. The lochial discharge was normal. Examination of the urine voided at my visit showed a cloudy, straw-colored fluid, which after being centrifuged

showed an abundance of leukocytes, bacilli (colon bacillus?), and a few epithelial cells, probably from the renal pelvis.

Bimanual palpation of the uterus and adnexa revealed nothing abnormal, so that all suspicion of uterine infection could at once be done away with and a diagnosis of right-sided pyelonephritis was made. The treatment consisted of an absolute milk diet and 1 gram (15 grains) of urotropin four times daily.

The patient was seen three days later, when it was found that the evening temperature and the pulse were the same as upon my first visit; and the patient complained of a frequent desire to urinate. Bimanual vaginal examination increased this desire, and by a more careful palpation it at once became evident that the right ureter was painful along its entire length. There was less pain in the lumbar region, so that palpation of the kidney was rendered easier, the lower pole of the organ being distinctly felt, and when caught between the fingers gave rise to rather sharp pain. The same treatment was continued for five weeks, during which time the pulse and the temperature gradually returned to the normal, and the pus diminished in quantity, so that at the end of this time there was barely a trace, and the bacteria had entirely disappeared. Some months afterward I was informed by the physician that the patient had entirely regained her health.

Before affirming the reality of a descending infection, one should not forget that during labor, and especially at the time of delivery, entrance of bacteria into the urethra, whose mucosa becomes everted, is rendered easy by the eversion of the anal orifice.

A former cystitis, acute or chronic, latent or awakened, related or not to pregnancy, a primary or secondary infection produced by a dirty catheter, commencing in the bladder or propagated to the ureter, represent the various ways in which *Bacterium coli* may reach the kidney. When ascending infection is incriminated, it is not even necessary for the bladder to become infected before a ureteritis becomes established. The organism may remain in the bladder, leading a saprophytic life, and then extend upward along the ureter, this being favored by a temporary retention; then it enters the dilated ureter and renal pelvis, here encountering a point of lessened resistance, which is favorable to its development, the contrary being the case of the bladder.

The ascending infection has been doubted by many observers, who believe that such infection is probable only when there is absolute evidence of a vesical infection. But, on the other hand, what proves the reality of an ascending infection is that, in some instances, the same organism, primarily located in the kidney, is continually thrown into the bladder with the urine, and still no infection of this viscus takes place, while in other cases the organism enters the bladder, causing an ascending infection of the ureter and kidney without producing any infection of the urinary reservoir. Then,

again, it is well known that, in certain infections, the bladder constantly contains *Bacterium coli*, from the fact of retention, and still cystitis rarely develops. All this goes to show that *Bacterium coli* can pass through the bladder without leaving behind any traces of its presence that are clinically demonstrable.

*Bacterium coli* is far from being the specific agent of postpartum pyelonephritides, because it is the common factor of renal disturbances during pregnancy as well; this brings me to the question of the soil in which the pathogenic germ may grow. Clinically speaking, a woman who has just passed through labor represents a surgical case; there is a wound of the cervix, more or less extensive, and at least more or less contusion of the vagina and perineum. Without considering the loss of blood due to the raw surface left by the placenta, it should be recalled that the lochia represent an excellent culture medium for various bacteria. Intestinal atony, which is of frequent occurrence during pregnancy, reaches its highest point of intensity after delivery, no matter what may be its cause. This very constipation retains the intestinal bacteria within the gut, so that the infectious agents may easily enter the blood current, and in the cases I am now considering it has been shown that *Bacterium coli* can enter the kidney by the renal artery. Vesical inertia does not have as bad an influence on the organism as intestinal atony, but it is a very marked predisposing cause for infection from the catheter or other bladder instrumentation.

If the patient nurses the child, it is evident that this weakens the organism generally on account of the removal of a certain amount of nutritive substances which go to manufacture the milk. In other words, the new mother may be looked upon as not in absolutely normal health for the above-mentioned reasons, and from this very fact, she is more susceptible to develop morbid phenomena if the occasion presents itself.

The cause of pyelonephritides occurring in the puerperium may be summed up briefly as follows: Labor is over and the uterus is about to commence its arduous work of retrogression, the maximum activity of which is probably between the ninth and twelfth days. Measurements taken by Varnier, Zinsstag, and others have shown that, the bladder being empty, the height of the uterus above the pubis is 13 cm. the second day postpartum, 6.5 cm. on the ninth day, and 5.5 cm. on the twelfth day. This decrease in height is due to a diminution of the uterus resulting from an incomplete atrophy of all the elements forming the uterine walls before pregnancy which have become hypertrophied by gestation; secondly, there is antelexion of the uterus. The apparent regression is greater than in reality, and is principally due to an exaggerated uterine antelexion, because after the fifth day the uterus will have taken on the shape of a non-pregnant organ, its corpus, being directed according to the axis of the superior strait, is perpendicular to the vagina.

Now, at this time, as the corpus uteri is nearly in the axis of the superior strait, it can compress those organs which lie behind it, and this is all the easier from the fact that after labor most women are kept in a horizontal position, a condition which pushes all the abdominal viscera backward. Now, the ureter passes exactly over the sacro-iliac symphysis, and a very mild compression can result in its complete obliteration. According to the experiments of Ludwig and Löbel, the pressure of the urine in the renal pelvis and ureters is always very low, and does not appear to reach above 10 mm. of mercury. This conclusion has been confirmed clinically, two cases of hydronephrosis due to compression of the ureter by an abnormal branch of the renal artery having been recorded by Le Dentu, while Young, of Baltimore, not long ago, published the case of a stricture of the ureter resulting from a mere compression by an inflamed seminal vesicle. Now, the weight of a uterus undergoing involution varies between 300 and 600 grams from the eighth to the fifteenth day postpartum. By its convex posterior aspect it lies on the ureters, which are dilated from the recent pregnancy, as has been proved by numerous writers, and having incompletely returned to their normal caliber, a fact which increases their surface of compression, no matter how small may have been this temporary dilatation. For that matter, this compression of the ureters does not belong to pregnancy and the puerperium alone, because it may result from any kind of pelvic tumor, and we all know that there are many renal complications arising during the progress of uterine carcinoma resulting from compression or obliteration of the ureters from the neoplasm. Uterine fibromas, ovarian cystomas more rarely, may compress the ureters and be the starting point of renal lesions. Consequently, during the puerperium, the uterus may compress the ureters and thus set up a pyelonephritis.

There are also two other ways of explaining the development of this renal complication, the first being the persistency of a condition of lessened resistance created during pregnancy by compression of the ureters by the pregnant uterus; in this respect, I believe the following case may be taken as an illustration: The patient, married at twenty-six years of age, became pregnant twenty-one months later. The pregnancy, during the latter months, was complicated by phenomena of auto-intoxication, although the urine remained perfectly normal. The patient complained of rather severe headache, marked constipation, cedema of the ankles, and disturbances of sight. For this reason, she was at once put upon an absolute milk diet, which resulted in a notable diminution of the symptoms. The uterus was unusually developed and lay decidedly to the right side of the abdomen. Labor occurred at term, and was perfectly normal.

The first few days following labor presented no incident worthy of note; micturition was normal. On the sixth day the temperature,

which had been perfectly normal, suddenly rose in the afternoon to 39.5° C., accompanied by a severe chill. The tongue became coated, the abdomen somewhat distended and generally painful, but a careful examination showed that the greatest amount of pain could be elicited in the right renal region. An examination of the urine at this time showed that it contained some pus cells and quite a number of red blood corpuscles; also some bacteria. As far as the uterus and adnexa were concerned, they were absolutely normal, the lochia having its accustomed odor and being discharged in proper amount. Two days later the urine became decidedly purulent, and the pain became localized in the region of the right kidney; consequently a diagnosis of pyelonephritis was made. During the next week the amount of pus in the urine increased; red blood corpuscles were also present, and bacteria, which in the hanging drop appeared like the colon bacillus, were evident. The temperature at the end of the week had reached 40.2° C., and the pulse was becoming filiform and reached 120. The patient presented all evidences of having a large focus of pus in the abdomen, and it was, therefore, decided to cut down on the right kidney. This was done the following morning by transverse lumbar incision, and a large congested kidney with a considerably dilated pelvis was exposed. The organ was split open, and when the interior of the pelvis was reached a large phosphatic calculus was removed, which, after drying, weighed 47 grams, while the renal pelvis contained 50 c.c. of distinctly purulent urine. Other than the congestion the renal parenchyma appeared to be normal. Lumbar drainage was established and at the end of three months the patient was discharged well.

From most of the published cases it will be seen that pyelonephritis of pregnancy and the puerperium is usually right-sided, this being easily accounted for by the fact that the gravid uterus is more prone to lie toward the right, while it rarely becomes inclined toward the left. Cases of left-sided pyelonephritis, signifying that the ureter must have been involved in the first place, may be explained by the fact that the left ureter has been compressed during pregnancy, or that there is a continuation of the compression by the uterus undergoing subinvolution.

Although, during pregnancy, a differential diagnosis is most urgent, on account of the unfortunate influence that pyelonephritides may exercise over the mother and especially the child, it is, perhaps, quite as imperative during the puerperium, and here, certainly, it is much more difficult, because uterine infection is more likely to come to one's mind, in addition to appendicitis, typhoid fever, or some intestinal infection. In these cases, in which all the above-enumerated symptoms are present, especially pus in the urine, it seems that the solution of the problem should be easy, although uterine infection may be also present with ureteral and renal lesions without there being any connection between the two morbid processes.

Some diseases may simulate pyelonephritis, such, for example, as acute tuberculosis or typhoid fever, but I shall only here consider puerperal infection, appendicitis, and intestinal infection.

In considering the most important of these, puerperal infection, abdominal pain, elevation of the temperature, and a bad general condition are the symptoms common to both pyelonephritis and uterine infection. When these symptoms are met with, the first diagnosis that comes to one's mind naturally is puerperal infection. However, there are several characteristics of these symptoms which weigh in favor of pyelonephritis. These are the marked rise in temperature of  $2^{\circ}$  or  $3^{\circ}$  C., followed by a morning drop to the normal, or even below. The condition of the pulse is never in relation to the rise in temperature, while in puerperal infection the pulse follows the temperature curve, and is usually poor. In pyelonephritis the patient's general condition is good during the intermission of the temperature. There is nothing absolute, of course, in these differences, but they help to differentiate the diseases in many instances. When a kidney contains a certain amount of pus pent up in the pelvis, after a while the temperature and pulse will be as in any serious form of infection, and this was the case in the instance of pyelonephritis with calculus reported.

Pain in the lumbar region is not very marked in ordinary cases, and, therefore, the patient is not likely to complain of it. But all things taken into consideration, a differential diagnosis may be made even before the appearance of pus in the urine, if one will only recall pyelonephritis; this, as many other affections is not diagnosed simply because it is completely forgotten. As a practical conclusion of what has been said above, given elevation of the temperature during the puerperium, one should commence by a careful examination of the uterus and adnexa, and, having found that there is no lesion in the small pelvis, the possibility of a pyelonephritis should at once come to one's mind; a careful examination of the urine should be made, as well as a methodical palpation of the renal region and ureters, although the patient may be perfectly free from pain in these regions.

The next important differential diagnosis to make is that of appendicitis and pyelonephritis. If in a puerperal woman examination reveals nothing abnormal in the uterus and adnexa, and abdominal pain is present, with a rise in temperature and constipation (a frequent occurrence during the postpartum), the appendix should be immediately examined; not infrequently the region of McBurney's point will give rise to pain on palpation, from the fact of reflex pain along the ureter. The maximum point of pain will be found close to McBurney's point, for the simple reason that the course of the ureter is very near the former, and consequently an erroneous diagnosis of appendicitis may be made. I have not in mind here the very acute forms of appendicitis which are ushered in

by vomiting, high fever, peritoneal expression, and intense pain in the cecal region, with almost complete intestinal occlusion, because, under these circumstances, the diagnosis of the appendiceal lesion would be only too evident. In those cases in which there is any doubt as to the diagnosis of appendicitis, one should wait, always prepared to interfere should any change in the symptoms require operation. One will not be obliged to wait long, because a careful examination of the urine, kidneys, and ureters will quickly do away with the diagnosis of appendicitis, while that of pyelonephritis will be made. In passing, I would simply refer to those ordinary forms of intestinal infection which arise during the puerperium in women having chronic constipation. In these cases, as in pyelonephritis, the tongue is coated, there is a rise in temperature, and the patient complains of abdominal pain, but, here, again, careful examination of the urinary apparatus will soon settle the question of diagnosis.

A few words as to the examination of these cases. Palpation, which during the puerperium is much easier and gives better results than during pregnancy, will only give rise to one symptom, namely, pain. The renal pelvis and its ureter must reach quite a high degree of dilatation in order to be felt by bimanual palpation. One rarely, if ever, meets with these instances of calculous hydro-nephritis of long duration, and one is often struck by the contrast existing between the violence of the general reaction and the absence of any important tumefaction in the lumbar region. Ordinarily there is some muscular rigidity, but only on the diseased side; this is especially manifest when the intrarenal tension has become considerable, and it ceases or diminishes when the renal pelvis becomes emptied, thus lowering the tension. Vaginal examination per se gives little information, because the ureter is usually healthy in its intravesical portion, although in one of my cases it was distinctly palpable. But even when the ureter is not involved in its terminal portion, pressure made upon it near its entrance to the bladder may provoke a ureterorenal reflex, and occasionally, when all other signs are wanting, this alone has allowed one to make a diagnosis of pyelonephritis. The urine will always be found to contain pus, and the pyuria alone should be sufficient to indicate a pyelonephritis if the bladder itself is not the seat of any lesion. A symptomatic cystalgia may be differentiated from a true cystitis by the presence of a cloudy polyuria, absence of bladder pain on palpation, and by a normal sensitiveness to tension, because one should be able to inject from 150 to 200 c.c. of liquid into a normal bladder without setting up a desire to urinate. I would here point out that the amount of suppuration is in no way proportionate to the intensity of the infection; not infrequently the urine may be almost limpid, although the general symptoms are quite serious. Generally speaking, when the urine becomes very purulent the



temperature falls and the pain diminishes, from the simple fact that drainage is effective.

Ureteral catheterism and intravesical segregation of the urine are very important in order to ascertain if one or both kidneys are involved, and, during the puerperium, their undertaking is far less difficult than during pregnancy.

If, as I have endeavored to show, pyelonephritis occurring during the puerprium should be particularly differentially diagnosticated from puerperal infection, it may be asked whether or not the former, on account of the extension of the pathogenic bacteria giving rise to it, may not produce the latter. Consequently, the prognosis of pyelonephritis manifesting itself during the puerperium should be considered from the point as to whether or not the urinary infection may finally involve the genital apparatus, secondly, from the renal viewpoint, and, thirdly, from the question of nursing.

Referring to the first question, it will appear from cases recorded thus far that patients having pyelonephritis after labor are in no way contaminated, as far as their genital organs are concerned. This fact might, in the first place, appear strange when one considers how easily inoculation of the vagina and uterus might take place from the pyogenic agents contained in the urine. Perhaps the non-infection may be due to certain chemical differences between the purulent urine and the postpartum uterine and vaginal secretions, preventing the development of the bacteria contained in the urine. Then, again, it may be due to a careful protection of the genital zone in patients presenting urinary infection. However this may be, it seems to me, clinically demonstrated that the uterine and vaginal lesions of continuity arising during labor do not become infected by the urine. From the view point of acute renal infection, a cure is generally the outcome, but relapses of the renal process are prone to arise.

Two therapeutic measures can be resorted to in dealing with a pyelonephritis, whether during pregnancy or postpartum, namely, a medical and a surgical treatment. No comparison can be made between the two, because they have their own special indications, surgery being resorted to only in complicated cases.

The medical treatment consists essentially in rest in bed, a milk diet, and alkaline drinks combined with diuretics and urinary antiseptics. To relieve pressure on the ureters from the uterus, various positions to be assumed by the patient have been advised. Excellent results have been obtained by having the patient lie on the side opposite to that of the involved kidney, thus causing the uterus to fall over to the other side and away from the ureter which it compresses. Whether the lesions be on one side or bilateral, Lepage advises the patient to sit in a chair rather than lie in bed, because in the former position the uterus no longer brings all its weight to bear on the ureters and, consequently the compression is diminished.

For the infection of the kidney and ureter an absolute milk diet must be instituted. Salol, urotropin, and the balsams have their indications. When there is retention with infection, some favorable results may be obtained by distention of the bladder, as advised by Pasteau. It is well known that distention of the bladder produces an increase of the renal secretions, as well as of the contractility of the excretory apparatus. Therefore, Pasteau injects from 150 to 160 c.c. of tepid boric acid solution very slowly into the bladder; this is repeated three times a day, the patient being requested to retain the fluid in the bladder as long as possible. It should be pointed out that this treatment is absolutely contra-indicated when cystitis is present.

As to surgical treatment, nephrotomy is probably the only operation required, and from an examination of the literature it appears that it has rarely been necessary to resort to it. Nephrectomy, which is an extreme and radical resource, has never been required in cases of pyelonephritis occurring postpartum, so far as I am aware.

## THE ANATOMY AND PATHOLOGY OF THE CAROTID GLAND.

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THIS work was undertaken primarily to determine the effect of various systemic diseases on the carotid gland; incidentally, the anatomy and histology of the gland have also been closely observed. A review of the literature was given by Kohn,<sup>1</sup> in 1900, and by Funke,<sup>2</sup> in 1904. A summary of the cases of tumors of this organ, reported up to the time of their publication, was given by Keen and Funke,<sup>3</sup> in 1906. Therefore, it does not seem at present necessary to go over the literature, and I shall proceed to a description of my own findings.

**MATERIAL AND TECHNIQUE.** Human material was obtained as fresh as possible from the cadavers at necropsies performed in various hospitals of Chicago, and particularly the Cook County Hospital. Fifty human cases altogether were examined; and from animals killed at the Hull Laboratories and at Armour & Co.'s Union Stock Yards, material was taken for comparative study. Fixation was by Zenker's fluid.<sup>4</sup> In the first 22 human cases, and

<sup>1</sup> Archiv f. mikro. Anat., 1900, vol. lvi, p. 81.

<sup>2</sup> American Medicine, 1904, vol. viii, p. 109.

<sup>3</sup> Jour. Amer. Med. Assoc., 1906, vol. xlvii, pp. 469 and 566.

<sup>4</sup> Kohn recommends a mixture of formalin and potassium bichromate. Staining was done with Delafield's hematoxylin and eosin, Van Gieson's, and Mallory's reticulum stains.

in all animal material, pieces of tissue about an inch in average length, including the common, internal, and external carotid arteries, with some branches of these, were embedded in celloidin. The tissues were then cut at various levels of about 100 microns intervals, cutting three or four sections at each level, of about 12 microns in average thickness. The sections were stained with hematoxylin and eosin and search was made for the gland. On cutting blocks of tissue in this way, in many cases it was possible to tell by the naked eye whether the gland was at the level reached; it showed itself as a clump of tissue closely related to the outer coat of the arteries, pinkish white, sometimes lobulated, sometimes uniform, in appearance. Three kinds of tissues were constant sources of confusion: (a) A ganglion of the sympathetic nervous system, which is usually uniformly whitish in appearance, but is not closely adherent to the adventitia of the carotid bloodvessels. (b) A nerve trunk, the fasciculi of which on cross section resemble the lobules of the carotid gland; this nerve trunk was either the vagus or sympathetic; in the first instance it was not attached closely to the outer coat, and in no case was it found posterior or anterior to the bifurcation of the carotid artery, but occupied always the lateral side. When the nerve trunk was sympathetic it was sometimes cut obliquely, so that a lobular formation was not shown; it resembled a clump of connective tissue, which was not adherent, however, to the adventitia. (c) A clump of fibrous connective tissue, which is adherent to the adventitia, but differs generally from the carotid gland by the dead white color and its uniformly dense appearance; in several cases, however, the gland presented exactly the appearance described, and only microscopic examination decided the real nature of the tissue.

Therefore, in macroscopic examination of blocks of tissue cut transversely the points of differentiation were (1) pinkish white color; (2) lobulation or uniformity; (3) close relationship to adventitia, into which the capsule of the carotid gland seems to merge. The presence or absence of the gland was considered established only after a careful microscopic examination of the stained sections.

This method of finding the gland is very valuable, since sometimes the gland, either because it was very small or was concealed in the adventitia, escaped detection by macroscopic dissection. It is the only reliable method for finding the gland in lower mammals, since in these it is relatively small, and the surrounding connective tissue is much thicker and denser than in man.

Beginning with Case XXIII, the attempt was made to dissect out the gland, and in almost every case this could be successfully done. When it was located, either the gland alone or a piece of bloodvessel with it was embedded in celloidin or paraffin. In dissecting out the gland fresh material was always used, because hardening fluids tend also to empty the bloodvessels and capillaries and coagulate the tissues; thus the reddish appearance could not be well dis-

tinguished. It is not uniformly red, but rather mottled with light red and dark red points. In this dissection the gland is again to be distinguished from (a) connective tissue, which is paler, uniform, and can be broken into fibers; (b) lymph glands in the intercarotidal tissue, which are sometimes hyperplastic, although usually they cannot be seen. If they are hyperplastic, they are usually uniformly red in appearance and detached from the wall of the bloodvessels. In one case the carotid gland was found hanging from the external carotid artery by a fibrous stump, and was so surrounded with fat that it appeared very much like the lymphatic glands (which were enlarged in this case probably on account of tuberculosis of the lung); only its attachment to the artery guided me to keep the tissue for further examination, and to my surprise microscopically it turned out to be the carotid gland. (c) It also has to be distinguished from ganglia of the sympathetic, which are, however, of the white color of the nerve, are connected with the sympathetic cord, and not attached to the adventitia of the carotids.

**ANATOMY AND TOPOGRAPHY.** The carotid gland is generally described as a reddish ovoid organ of firm consistency, the longest axis being vertical, the upper pole broader than the lower, lying on the posterior surface of the bifurcation of the common carotid artery, and not constantly present in man. Funke states that he found it most frequently on the inner and posterior side of the internal carotid. Schaper<sup>5</sup> states that the gland is spindle-shaped, and that in man it is more regular in size and shape than in other mammals. Its size varies, according to different authors: Luschka<sup>6</sup> gives it as 7 by 4 by 2 mm., Schaper as 5 to 7 by 2, 5 to 4 by 1.5 mm. A fibro-elastic stump connecting the gland with the bloodvessel on which it lies, and carrying its artery, is described as the "ligament of Mayer." Most authors agree that there is only one nutrient artery springing from the one of the carotid arteries on which the gland lies. Henle<sup>7</sup> states that it receives two or three branchlets from the *carotis primitiva* (common carotid). Poirier and Charpy, speaking about the relation of the gland to the nerves, state that a great number of filaments surround it, either directly or after forming a plexus, the intercarotidal plexus, the filaments of which come from the superior cervical sympathetic ganglion, the *nervi molles* of Haller, the glossopharyngeal, hypoglossal, and superior laryngeal.

In my own experience I found the shape of the gland generally ovoid, in several cases rounded, and in a few elongated. In the majority of cases it was found single on each side of the neck. Luschka has observed the occasional splitting of the organ into two lobes, and my findings confirm his statement. The gland on the left side in Case XLI was remarkably flattened, and on the free edge there was

<sup>5</sup> Archiv f. mikro. Anat., 1892, xl, p. 287.

<sup>6</sup> Archiv f. Anat. u. Physiol., 1862, p. 406.

<sup>7</sup> Cited by Poirier et Charpy, Traité d'anatomie humaine, Paris, 1901, tome ii, p. 668.

a depression, which, however, was not deep enough to make the gland a uniform shape. In Case XXIX, on the left side, the gland was elongated and constricted at the middle, dividing it into two lobes

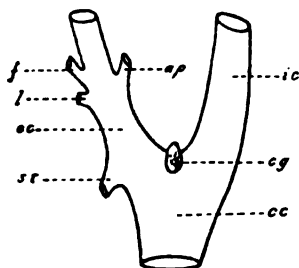


FIG. 1.

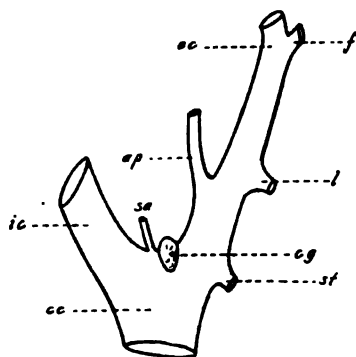


FIG. 2.

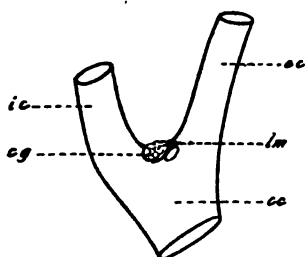


FIG. 3.

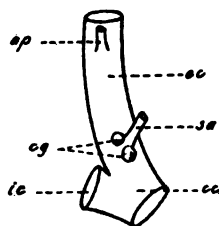


FIG. 4.

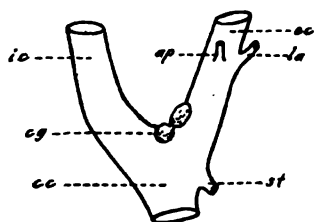


FIG. 5.

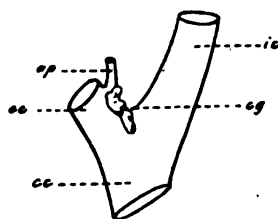


FIG. 6.

The carotid gland, posterior views, illustrating its gross anatomy and variations in location. Fig. 1. The most common form. Figs. 2-6. Several other types described in the text. Cc, common carotid artery; Ec, external carotid; Ic, internal carotid; Sa, small anonymous artery; Ap, ascending pharyngeal; St, superior thyroid; L, lingual; F, facial; Cg, carotid gland; Lm, ligament of Mayer.

united by an isthmus (Fig. 5). In Cases XXXV (Fig. 4) and XXXIII there were two distinct and well defined bodies on the left side. The gland was measured macroscopically every time that it was possible to do so, by carefully dissecting out the fat, including the connective tissue capsule and the glandular tissue in the mensuration. My measurements agree with those of other authors as to the variability of the gland in size. Out of twenty-six measurements, the average is 5 mm. in length, 3 mm. in breadth, and 2.5 mm. in thickness—an average diameter of 3.5 mm. The largest gland was 8 by 5 by 4 mm. The smallest was not detectable by naked eye inspection; only under the microscope was its presence established, and it was 0.5 mm. in diameter.<sup>6</sup>

As to the position of the gland, I also found it most commonly between the internal and external carotid arteries, resting posteriorly on the bifurcation of the common carotid, the ligament of Mayer being attached to the artery on which it lies (Fig. 1). Variations from the usual location are the following: In Case XXIV, on the right side, the gland was hanging by the ligament of Mayer to the outer side of the external carotid, 3 mm. above the bifurcation; in Case XXXI, on the left side, it was placed in front of the ascending pharyngeal artery, which arose at a lower level; in Case XXVIII, on the right side, it was a little elongated, placed upon the middle, not behind the bifurcation; in Case XXXVII, the right side was elongated, resting on the groove of the bifurcation superiorly and posteriorly, its upper pole being in close relationship with the ascending pharyngeal artery and deviating somewhat to the right of this, the lower pole resting posteriorly on the bifurcation (Fig. 6). In several other cases it was more intimately attached to the external than to the internal carotid. In one case the ligament of Mayer was not attached to the artery on which the gland was lying; the gland resting on the inner surface of the internal carotid about 1.5 mm. above the bifurcation, while the ligament of Mayer, with its contained bloodvessel, stretched across the intercarotid space, to be attached to the external carotid, into which the carotid gland artery opened (Fig. 3). In 5 cases (on only one side in 3 cases, and on both in 2) a small artery sprang from the bifurcation of the common carotid, and in every case the gland was intimately related to it, either embracing or directly adjacent to it (Fig. 2). Of the two lobules of Case XXXV, the one was anterior, the other lateral to this small artery (Fig. 4). I am not aware of any name given to this artery.

The gland was found only once in 8 human fetuses examined by Funke, who apparently examined no adult material. Out of 50 human cases of my own it was found present in all but 5. In 4 cases it was found only on one side, and in 1 of these last cases the only

<sup>6</sup> The gland increases in size as the individual grows, from proliferation of the parenchyma, bloodvessels, and connective tissue.

carotid body present was much enlarged (about 5 mm. in average diameter), as though a compensatory hypertrophy had taken place.

Speaking of the comparative anatomy of the carotid gland, Schaper<sup>9</sup> concludes: "It is probably present in all mammals. A homologous organ is not found in birds, at least in the neighborhood of the bifurcation of the carotid artery. The so-called carotid gland of batrachians and salamanders is not homologous with the one in mammals. In fishes it has not yet been observed, but the *Axillarherzen* that Roehen and Haien found, and about which von Leydig wrote, are probably of the same nature." Kohn's findings confirm Schaper's conclusions. Funke was not successful in finding the gland in lower animals (cat, rabbit, and guinea-pig).

By taking pieces of tissue containing the bifurcation of the carotid artery and cutting sections at 100  $\mu$  intervals, I was able to find it in cats, dogs, oxen, goats, and monkeys. In these animals the gland in every case was too small for macroscopic dissection, and the connective tissue capsule was so thick and dense that no characteristic external appearance of the gland is shown. I agree with Schaper as to the variability of its position in mammals; in general it is placed posterior to the bifurcation, more closely attached to one artery than to the others. In the ox the gland was found somewhere in the neighborhood of the division of the common carotid artery into internal and external maxillary and occipital arteries,<sup>10</sup> and it was divided into two separate lobes.

**EMBRYOLOGY AND HISTOLOGY.** There are three theories as to the embryology of the carotid gland (see Keen and Funke): (1) Endodermal, which holds that the gland is derived from the third or fourth branchial cleft, as is claimed by Stieda, Rabl, Pierre du Meuron, and others. (2) Endothelial, as is believed by Katschenko, and confirmed by Paltauf and Szymonowickz, from the endothelium of the carotid artery, the first sign of the gland being a cellular thickening in the adventitia of one of the bloodvessels. (3) Nervous, propounded by Kohn, on account of his having found chromaffin cells corresponding to those in the sympathetic ganglia, and he says it belongs to a category of its own. The nervous origin was long ago suspected by Luschka, on account of its close relationship to the sympathetic nervous system, thus resembling the pituitary body, the suprarenal gland, and the coccygeal body.

Luschka first described the histological structure of the carotid body, and concluded that it is glandular, made up of tubules and vesicles, the formed elements being molecular masses with naked nuclei and cells, the nucleus being partly dark, partly granular, with a nucleolus, the cells being mostly elongated, and also polygonal or irregular, showing sometimes great similarity to cylindrical epi-

<sup>9</sup> Archiv f. mikrö. Anat., 1892, xl, p. 287.

<sup>10</sup> Martin. Lehrbuch der Anatomie der Haustiere, 1904, vol. ii.

thelium. Arnold,<sup>11</sup> on the other hand, held that the gland is of glomerular structure, and states that the tubules and vesicles of Luschka were only apparent; he believed free cells, nuclei, and molecular masses were not present.

Both authors were partly right, however, as is found by recent investigations, and now it is considered established that the gland is made up essentially of two parts: (1) Capillary bloodvessels, richly anastomosed, forming a sort of tuft; and (2) cells, epithelioid in character, situated in the interstices limited by the bloodvessels. The gland is surrounded by a dense fibrous (white and elastic) connective tissue capsule, from which prolongations are sent in, dividing the gland into lobules, which are again divided by delicate strands of connective tissue, inclosing the "Zellballen" of Schaper. It is maintained by Marchand<sup>12</sup> that there exists a hilum structure where the artery enters the gland, and then gives up one branch for each lobule, which in turn is broken up into capillary glomeruli, around which the formed elements are arranged. The efferent vessels from these tufts are gathered at the periphery of the organ into wide, thin-walled veins. The capsule contains both medullated and non-medullated fibers. Ganglion cells are scattered and few in number. Paltauf<sup>13</sup> found a connective tissue reticulum, which is regarded as a postmortem alteration by Schaper.

The formed elements are described as cells with cuboidal, polygonal, sometimes irregular, outline, similar to epithelium, with rounded or oval intense staining nucleus, often eccentrically placed, and containing a nucleolus. Mönckeberg describes an angular form of nucleus. The protoplasm is somewhat granular and small in amount. Frey<sup>14</sup> likens the parenchyma to the plasma cells of Waldeyer. I have observed very carefully the cells stained with hematoxylin and eosin and fixed in Zenker's fluid, and two types of cells seem to be evident in most cases. The protoplasm of each kind is similar in character, and they differ principally in the character of the nucleus. In one (type I) this is large, rounded or ovoid, vesicular, with chromatin granules distinct, and a dot of chromatin or nucleolus at the center. In the other (type II) the nucleus is smaller, similar to the lymphoid cell nucleus, rounded, dense, uniformly dark blue stained, with the distinct chromatin granules. In the majority of cases the cells of the second type predominate, in a few those of the first. In cases in which the cells were only of one type, the second type was the one present.

Among the cells of the "cell balls" and in the stroma, Stilling<sup>15</sup> found a kind of cell which stains brown by neutral salts of chromic acid. Kohn confirmed Stilling's observations, and calls these

<sup>11</sup> Virchow's Archiv, 1865, vol. xxxiii, p. 194.

<sup>12</sup> Virchow's Festschrift, 1891, vol. i, p. 537.

<sup>13</sup> Ziegler's Beiträge, 1892, vol. xi, p. 266.

<sup>14</sup> Cited by Kohn.

<sup>15</sup> Cited by Paltauf.



"chromaffin cells." Similar chromaffin cells are present in the adrenal, and some authors consider the chromaffin substance to be the cause of the effect of the gland extract upon blood pressure.

Recently Mulon<sup>16</sup> succeeded in producing a rise of arterial blood pressure, and sometimes an acceleration of the beat and force of the heart, by injecting watery extracts of the carotid gland of horses into the viens of rabbits, and he attributes this effect to the chromaffin cells of the gland. I tried on a cat two injections of glycerin extracts of equal quantities of material from human carotid glands, and I found invariably a *lowering* of blood pressure. These experiments will be repeated as soon as a suitable amount of material is obtained, and a more detailed account will be published later.

Concerning the relationship between the parenchyma cells and the capillaries, authors divide themselves, Reclus and Chevassu<sup>17</sup> say, into two sides. Some, with Eberth, Marchand, and Paltauf, see between the cells and the capillaries a very intimate relationship, the epithelioid cells being outgrowths from the vascular epithelium, and cite the endothelial origin of the gland as a support of their contention. Others, with Luschka and Stilling, consider that between the vessels and cells there is a true independence; they liken the carotid body to the suprarenal gland, the carotid body deserving at all points the name of blood vascular organ, and cite the endodermal origin of the gland for their support. Kohn says it is neither a gland nor entirely an epithelial structure, but belongs to a category of its own.

In my own cases, when the capillaries were found greatly distended with blood, the relationship between the epithelioid cells and the capillaries was more intimate, and they appeared to line the capillary lumina directly. When the bloodvessels were empty, however, fine fibrils of connective tissue seemed to separate the epithelioid cells from the endothelial lining of the capillaries.

In lower mammals Schaper found that the connective tissue of the carotid gland is less in amount than in the human, and he likens them to the younger stages of human carotid body. Kohn<sup>18</sup> describes four types of carotid gland, according to the degree of development of the connective tissue and the degree of division of the parenchyma. (1) "Compact type," a good example of which is the organ of the cat, which is characterized by fine interstitial connective tissue, so that the cellular appearance is more pronounced and a more parenchymatous constitution is shown. (2) "Lobular type," in which a greater amount of connective tissue divides the gland into lobules, pronounced in apes (*macacus rhesus*). (3) "Granular type," in which further subdivision of lobular into small granules (Zellballen) occurs, through an increased amount of connective

<sup>16</sup> Archives gén. de médecine, 1904, p. 3265.

<sup>17</sup> Rev. de chir., 1903, vol. xxviii, p. 157.

<sup>18</sup> Loc. cit.

tissue; this is the human type. (4) The "diffuse type," in which the cells are arranged in small globular groups, or small short strings, lying apparently independent of each other in the connective tissue; this type is present in rabbits.

My findings agree with those of Schaper in regard to the relative amount of connective tissue. In addition, it was noticed that the carotid gland of the mammals observed contained only one kind of cells, cuboidal in shape, with the nucleus large, rounded, and vesicular, showing distinct chromatic granules and a nucleolus; hence, they correspond to type I of the cells found in human glands. In general it may be said that the carotid gland of the cat, dog, goat, ox, and monkey in my cases had more of a parenchymatous appearance than in man. In the goat, monkey, and cat it is of a more compact type. In oxen the gland appears of a granular type, little individual groups of cells in more of an alveolar arrangement, and separated by fine strands of connective tissue. The dog's carotid gland has a greater development of connective tissue, and approaches to the young human gland in appearance, while the others (goat, monkey, cat, and ox glands) are more parenchymatous than in young stages of the human gland. In monkeys, at about the bifurcation of the carotid artery, a lymphatic gland is constantly found, which was at first thought to be the carotid gland.

**PATHOLOGY.** Only tumors of the carotid gland have been reported so far. I am not aware of any description of other diseases of this organ.

**Tumors.** The increasing number of cases reported within the last few years, and the possibility of mistake in the diagnosis of tumors of the neck, make one suspect that these tumors are not so infrequent as was formerly believed. Keen and Funke collected 29 cases: 27 observed in the living, and 2 discovered on autopsy. Hutchinson's<sup>19</sup> 8 cases of "potato tumors" are probably newgrowths of this kind. Their etiology is unknown; some coincidences with other diseases, such as tonsillitis in one case, buccal phlegmonous inflammation following extraction of a tooth in another, have been mentioned in attempting to indicate the ultimate exciting causes, but there does not seem to be enough foundation to attribute any special significance to these facts. There is no sex influence. They occur particularly in adolescence and adult life, cases having been observed from the eighteenth to the sixtieth year, mostly about the thirtieth. V. Heinleth<sup>20</sup> attempts to explain their formation by stating that the carotid body develops until puberty, when it either atrophies or development is arrested; if it continues to grow, a tumor is formed.

The tumors are usually oval in shape, the size varying from a pigeon egg to a goose egg. The consistency is variable, but it is

<sup>19</sup> Illustrated Medical News, October 18, 1888, and also November 3, 1888.

<sup>20</sup> Münch. med. Woch., 1900, vol. xlvii, p. 899; and also Cent. f. allg. path. u. Path. Anat. 1900, vol. xi, p. 599.

usually moderately hard and elastic. The color varies from a red-dish gray to a gray or brown. There is always a fibrous capsule which sends septa into the tumor. There are much enlarged veins on the surface, and the bloodvessels are so abundant that a sponge-like appearance is shown on the cut surface. They are usually intimately adherent to the common carotid artery and its branches, but in a few cases they could be peeled off easily. It can be said that their histology shows hyperplasia of the cells around the bloodvessels and the name of endothelioma is most generally accepted, since the most accepted embryological view of the origin of the gland at present is endothelial. The connective tissue septa are apt to undergo hyaline degeneration. The tumor cells are cubical, spindle, triangular, or polydehral in shape. Some have found processes from the angular cells, which seemed to be intimately connected with the capillaries. Chromaffin cells are also found, either in the alveoli or in the stroma. Some fuchsinophile cells are described by Keen and Funke.

The tumors are benign in the early stages; later they grow very rapidly, and not until then do they usually come to be noticed by surgeons. They have a marked tendency to adhere to the surrounding structures, the pneumogastric, the sympathetic, the hypoglossal, and the lingual nerves. In 1 case the tumor was adherent to the anterior surface of the cervical vertebræ; in 2 it reached the base of the skull; in another it bulged into the pharynx. In 5 cases there was enlargement of the neighboring lymphatic glands; in 1 other metastases in the liver were found postmortem; in another the growth was distinctly malignant, rapid wasting occurred, and the patient died without operation. In 4 cases there was recurrence after operation, probably on account of the incomplete removal of the cells of the gland.

*Sclerosis.* By this term is meant an increase of connective tissue of the carotid gland. This occurs in old age and in patients with syphilis of the carotid artery, whereby an arteriosclerosis is produced. Schaper found that in old age spontaneous dissolution of the cells and increase in connective tissue and bloodvessels occur. Careful examination of all the specimens I obtained, taking into consideration the age of the individual and the amount of connective tissue and sclerosis in the intima of the corresponding carotid artery, revealed the fact that sclerosis of the gland is always associated with sclerosis of the intima of the carotid artery, and the former is proportional to the latter. The process seems to start from the adventitia of the carotid artery, for the interlobular septa first increase in volume, thickness, and proliferative activity, as shown by round cells, elongated endothelioid cells, spindle-shaped cells, and young strands of fibrous connective tissue. In young individuals the connective tissue is very slight in amount, the cell balls seem to fuse with each other, and even the lobules are not very well defined. As

age, or, what is similar, arteriosclerosis, advances, proliferative changes take place, and the interlobular and intralobular connective tissue becomes more evident, separating the elements of the gland into lobules and cell balls; when arteriosclerosis becomes more marked the connective-tissue elements preponderate, the blood-vessels of the interlobular septa become sclerosed, the cell balls atrophied, and eventually the connective tissue, becoming denser and denser, undergoes hyaline degeneration.

Arteriosclerosis produced by syphilis in one case offers an instructive picture.

**CASE XXXIII.**—Male, aged forty-six years.

*Anatomical Diagnosis.* Aortic insufficiency and syphilitic aortitis.

*Gross Description of the Gland.* Only the carotid gland of the right side was obtained. It is made up of fairly distinct lobes, connected with each other by a fibrous vascular band. The larger one is on the posterior surface of the bifurcation, size 8 by 5 by 4 mm., a great deal larger than normal; smaller one located posterior to the internal carotid artery; size 3 by 2 by 4 mm. The arteries are thickened, and patchy calcification of the intima is present. Careful search for the opening of the artery into the carotid body failed to locate it.

*Histological Description.* The majority of the parenchyma cells are of the small type, with densely staining nuclei. A very striking amount of proliferative changes in the connective tissue, which is very cellular (lymphoid cells, endothelioid cells, and spindle-shaped cells) is present. The cell balls are well bounded by fibrocellular connective tissue. The cells of the stroma are increased, and in fact they seem to predominate, in the cell balls. The bloodvessels are not thickened, on the contrary, they seemed to be thinned by the great bulk of blood that they contain. As the opening of the main bloodvessel of the carotid gland is obliterated and no necrosis of the gland followed, it may be concluded that a good anastomosis with the vasa vasorum took place.

*Cloudy Swelling.* It was expected that the carotid gland would be affected by toxins and bacteria in the blood. I examined 11 cases of acute and chronic nephritis, 2 of septicemia, 1 of typhoid, 7 of pneumonia, and 2 monkeys (obtained from Dr. H. T. Ricketts) which died of Rocky Mountain Spotted Fever. These infectious and toxic processes, taken as a whole, had very little effect on the carotid gland. Only in one case was a marked change observed.

**CASE L.**—Male, aged sixty-four years; autopsy twelve hours after death.

*Anatomical Diagnosis.* Lobar pneumonia.

*Gross Description.* Only the right side was examined. Gland was about 2 mm. in diameter, placed posteriorly on the bifurcation. It looked small and sclerosed.

*Histological Appearance.* Gland sclerosed. The parenchyma under low power shows indefinite, dark-staining patches; with high power the parenchyma cells are seen to be somewhat swollen, more distinctly granular, boundaries altogether obliterated, fusing into one degenerated mass with scattered dark nuclei. This is cloudy swelling, but it does not extend to all the cell balls.

In several cases of septicemia the blood was laked, showing the effect of infection, and yet the cells of the gland seem to have altogether escaped pathological alteration.

*Hyaline Degeneration.* In tumors, hyaline degeneration of the connective tissue has been described by Keen and Funke, Monckeberg, Paltauf, and Kopfstein,<sup>21</sup> due probably to fusion of the fibers and subsequent homogeneous appearance.

As the gland grows older, the connective tissue increases in volume and density, and eventually becomes homogeneous in appearance, and hyaline degeneration takes place. This was particularly marked in Case XLIV (a male, aged forty-five years, dead of septicemia) in which the connective tissue made up half of the volume of the gland.

*Other Changes.* In Case XXXVII, a male, aged fifty-seven years, dead of chronic nephritis, there was found one very curious lobule. This was choked full of lymphoid cells, which were rounded in shape, poor in protoplasm, with dark, rounded nuclei without visible nucleoli. These must have sprung from the preëxisting connective tissue cells and from the blood stream, since neighboring bloodvessels showed slight increase of lymphocytes. In this particular lobule there were a few parenchymatous cells scattered here and there, as though the round cells had grown in among them and pressed them apart.

Four cases of miliary tuberculosis, and 4 of other kinds of tuberculosis were examined. In one case, a male of about twenty to twenty-five years of age, the tuberculosis was so generalized that even the intima of the arteries seemed to be riddled with millet seed tubercles; and yet in this case, as well as in all the rest, the carotid gland escaped infection.

Examination of glands from the following showed no pathological alteration: One case of multiple myeloma involving the frontal lobe of the brain, 1 case of pseudoleukemia, 1 of glioma of the brain, 1 of glioma of the retina, 4 of heart disease, 1 of gas poisoning, 1 of unknown poisoning, 1 of aortic aneurysm, 3 of cerebral hemorrhage.

*Postmortem Changes.* Schaper says that the cells contain a delicate hyaloplasm, and it is hard to preserve them true to life. This is the experience of all subsequent investigators. Comparing the animal material which was fresh, and the human material which was

<sup>21</sup> See Keen and Funke

obtained a varying length of time after death, I came to the conclusion that the granules of the protoplasm in the latter seem to dissolve at the periphery, and consequently they are relatively more granular toward the centre around the nucleus, and poorly defined vacuoles are formed apparently by dissolution of these granules. With longer standing, the protoplasm stains very poorly, the edges being ragged in appearance. I had cases examined up to six days postmortem, and the cells do not seem to dissolve entirely, as in the case of the medullary substance of the suprarenal capsule.

**SUMMARY.** 1. The carotid gland is variable in size, shape, position, and number; it is not always present, or at least cannot always be found in its usual location, and may be absent on both sides or only on one side.

2. It is probably present in all mammals, and is more of a parenchymatous character and more intimately embedded in the adventitia of the carotid arteries in the lower animals than in man.

3. It increases in size as the individual grows, because of increase of connective tissue, bloodvessels, and parenchyma. Reaching a certain stage, between twenty and thirty years, it remains stationary for a time, and then only the connective tissue increases, the interlobular bloodvessels thicken, and sclerosis and atrophy of the gland result.

4. There are two types of parenchyma cells, differing mainly in the amount of chromatin and the size of the nucleus. The parenchyma cells of lower mammals are only of one type, which is more similar to the type in man which is characterized by a large rounded vesicular nucleus.

5. The sclerosis of the gland is proportional to the sclerosis of the intima of the carotid bloodvessels, whether due to age or to syphilitic endarteritis.

6. The gland is not very much affected by systemic diseases, the only changes found being one case of cloudy swelling, one of lymphoid infiltration, and frequently hyaline degeneration of the sclerosed stroma in old age.

7. The cells undergo postmortem changes readily, but do not dissolve entirely, as do the cells of the medulla of the suprarenal.

8. The nature of my material was such that no conclusions can be drawn concerning the chromaffin cells.

This work has been suggested by and done under the supervision of Dr. H. Gideon Wells. Drs. Le Count and Bassoe and Mr. Rosenberg have provided facilities for the obtaining of material. Dr. Warren H. Hunter kindly allowed me to get material from his numerous autopsies. To all of them I wish to express my deepest gratitude.

## CONGENITAL UNILATERAL ABSENCE OF THE UROGENITAL SYSTEM AND ITS RELATION TO THE DEVELOPMENT OF THE WOLFFIAN AND MUELLERIAN DUCTS.

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THE occurrence of congenital absence of the urogenital system is not so uncommon as to detract from the interest of such a case. Although instances have been mentioned by Aristotle, Vesalius (1543), Lopez (1564), Columbus (1572), Bauhinus (1621), Laurentius (1628), Duretus (1635), Riolanus (1648), and Eustachius (1707), they are quite uncertain, as no distinction has been drawn between atrophied, fused, and undeveloped kidneys.

Mosler<sup>1</sup> is among the first of the modern writers to take up this subject in a systematic manner, and he has tabulated 14 cases of absence of the kidney; in 7 of these the ureter had failed to develop, while in 2 the kidney was but rudimentary.

Beumer<sup>2</sup> collected 48 cases between the years 1853 and 1878, and in 44 of these the kidney was completely absent, while in 4 it was rudimentary. He found that genital defects were present in 13, 8 females and 5 males. In 3 of the males the seminal vesicles and vas were both absent, and in 1 the testicles also; in the other the normal genitals were present, but in addition there existed a 38 mm. vagina and a 25 mm. uterus, on the right side. In the females the malformations of the genitals consisted chiefly of bicornate uterus, and absence of one tube or one-half of the uterus or vagina. The ovaries were present in all cases. Schwengers,<sup>3</sup> in 1881, mentions a case of absence of the left kidney and ureter, and Thibierge,<sup>4</sup> the absence of the right kidney and ureter in a boy aged nine and a half years. Greenfield<sup>5</sup> describes 2 cases of absence of kidneys and ureter in 1 of which there was also absence of the testicle, vas, and vesicles on the affected side. Mention may also be made of Murchison's<sup>6</sup> case of absence of the left kidney, Hillier's<sup>7</sup> left kidney, Bruce's<sup>8</sup> left kidney and ureter, and both Kelly's<sup>9</sup> and Duckworth's<sup>10</sup> left kidney. Coen,<sup>11</sup> Guttmann,<sup>12</sup> Bartscher,<sup>13</sup> Ogsten,<sup>14</sup> and Gatti<sup>15</sup> report similar cases. Lamiere<sup>16</sup> cites the absence of a kidney in an

<sup>1</sup> Arch. der. Heilk., Jahr., 1863, iv, p. 289.

<sup>2</sup> Berl. klin. Woch., 1881, p. 481.

<sup>3</sup> Trans. Path. Soc. London, 1884, vol. xxviii.

<sup>4</sup> Ibid., vol. xv, p. 46.

<sup>5</sup> Ibid., vol. xix, p. 274.

<sup>6</sup> Vide Ballowitz, 22.

<sup>7</sup> Vide Brown, 21.

<sup>8</sup> Cited by Brown, 21.

<sup>9</sup> Virch. Arch., 1878, lxxii.

<sup>10</sup> Prog. med., vol. x, p. 666.

<sup>11</sup> Ibid., vol. x, p. 190.

<sup>12</sup> Ibid., vol. xvii, p. 175.

<sup>13</sup> Trans. Lond. Path. Soc., vol. xx.

<sup>14</sup> Arch. f. path. Anat., 1883, vol. xxii.

<sup>15</sup> Obst. Soc. Lond., 1880, vol. xxi, p. 57.

<sup>16</sup> Jour. de Sci. Méd. de Lille, 1892.

individual aged sixty-four years. Coen found, in a study of 33 monstrosities, that the kidney was absent in 15 and the adrenals were larger than normal. Gubbins<sup>17</sup> reports the absence of the left kidney, ureter, and adrenal, and Mackey<sup>18</sup> a single (right) kidney in a child aged two years and nine months. Eschaquet<sup>19</sup> describes the non-development of the left kidney, ureter, ovary, and tube, and one-half of the uterus. Rayer<sup>20</sup> cites 17 cases and in 12 of these the ureters and vessels were not present. Tweeding<sup>21</sup> describes the absence of the right kidney, ureter, and vessels in a woman aged thirty years, while M. Brown<sup>22</sup> reports 3 cases in 12,000 autopsies.

Ballowitz<sup>23</sup> was the next writer to collect cases of this condition. Up to 1895 he computes 213 cases, and states that there are probably 25 more, which represent literature to which he had not access. I have been able to trace some of the latter cases, and the results will be noted later. Ballowitz describes 3 cases of his own. In the first there was no trace of the left kidney, ureter, or vessels, but the adrenal was present; the left vas, seminal vesicles, and ejaculatory duct were missing and the testicle atrophic. In the second the right kidney was wanting, and in addition the ureter and vessels; the genitals, however, were normal. In the third the left kidney, ureter, vas, and ejaculatory duct were absent, and the testicle soft and smaller than usual.

From a study of the 213 cases Ballowitz found that the left side was more commonly affected than the right, in the proportion of 117 to 88, with 8 undifferentiated. This condition occurred more often in the male than in the female, and here on the left side oftener than on the right, 70 to 42. In the female the proportion was nearly even. Usually rudimentary vessels were found, and in all but 15 the ureters were undeveloped. There was the usual compensatory hypertrophy of the remaining kidney. Of the 213 cases, in only 103 was there any mention made of the genitals. In only 73 were there any defects; 41 occurred in the females and 28 in the males; in 4 the sex was not mentioned. The efferent system, derivatives of the Wolffian and Muellerian ducts, seemed more commonly affected while the ovaries and testicles showed little alteration.

In 18 the uterus was bicornate (10 right and 8 left); in 5 the uterus and tubes were both absent; in 10 the uterus was bicornate and contained a double cavity, while in 2 a double vagina existed. In 3 cases alone were the ovaries on the affected side absent. The external genitals were seldom altered.

In the male the vas and seminal vesicles were usually affected. Both were absent in 13, while in 2 the vas was wanting and the

<sup>17</sup> Brit. med. Jour., January, 1883, p. 115.

<sup>18</sup> Prog. med., Paris, 1875.

<sup>19</sup> Jour. Anat. and Physiol., 1893-94, vol. xxviii.

<sup>22</sup> Ibid., p. 194.

<sup>18</sup> Ibid., September, 1887, p. 626.

<sup>20</sup> Traité des Mal. des Reins, 1841.

<sup>21</sup> Virch. Arch., 1895, vol. cxli, p. 309.



vesicles atrophic; in 3 the vesicles alone were absent, while in only 4 was the ejaculatory duct missing. In 2 the testicles were entirely wanting, while in 8 they were small and atrophic.

The following are among the doubtful cases of Ballowitz, and these have been confirmed by the writer. Darby<sup>24</sup> found an absence of the left kidney and ureter; Thatcher<sup>25</sup> mentions 2 cases of absence of the kidney and ureter, but makes no mention of the genital defects, sex, or side affected; in the same meeting Armstrong<sup>26</sup> stated that he had seen such a defect in a man. Peabody<sup>27</sup> cites 2 cases, 1 of the right kidney and ureter and the other of the left kidney and ureter and the presence of a uterus bicornis. Isaacs<sup>28</sup> noted the absence of the left kidney and ureter in a child of three months; Polk<sup>29</sup> found the right kidney missing, postmortem, in an individual in whom the left had been removed for disease; in addition he found the right ureter, vagina, and uterus absent, but both ovaries were present. Holt's<sup>30</sup> case was that of a rudimentary, cystic kidney, and therefore cannot be counted. Wier<sup>31</sup> noted the absence of the left kidney and ureter, and Church<sup>32</sup> mentions the same defect in a female, and states that he had seen another such case at an autopsy. Ingals<sup>33</sup> found the right kidney wanting in a female, while Gouley<sup>34</sup> noted a single pelvic kidney, apparently the right, that received its blood from the middle sacral artery. Cargill<sup>35</sup> merely mentions the absence of the left kidney in a male, while Hutchinson's<sup>36</sup> case represents a cystic kidney. Several references given by Ballowitz were incorrect, and the remainder could not be obtained.

In addition to the above, I should like to note some cases overlooked by Ballowitz. Tweeding's case was one of absence of right kidney, ureter, and vessels in a woman aged thirty years; Dr. Fenby<sup>37</sup> and Dr. Walker mentioned a case in which no trace of either right kidney or ureter could be found, while Dr. Falk<sup>38</sup> cites one in which there was absence of the right kidney and ureter. Prudden,<sup>39</sup> in his discussion of Holt's case, says that all cases that he had reported showed absence of the left kidney. Church<sup>40</sup> mentions 2, while Ballowitz gives him credit for only 1. Since 1895 Newman<sup>41</sup> reported absence of left kidney, ureter, and vessels; Sunderland<sup>42</sup>

<sup>24</sup> Proc. Phila. Path. Soc., 1857 to 1860, p. 199.

<sup>25</sup> New York Med. Record, 1892, vol. xlii, p. 517.

<sup>26</sup> Ibid., vol. xlii.

<sup>27</sup> Bull. New York Path. Soc., 1881, p. 138; New York Med. Record, 1882, vol. xxii.

<sup>28</sup> New York Jour. of Med. and Collat. Sci., 1858, p. 218.

<sup>29</sup> New York Med. Jour., 1883.

<sup>30</sup> New York Med. Jour. and Rec., 1887, vol. xxx, p. 696.

<sup>31</sup> Indian Med. Gaz., 1872, vol. vii, Calcutta. <sup>32</sup> Jour. Amer. Med. Assoc., 1884.

<sup>33</sup> Chicago Med. Jour. and Examiner, 1875, vol. xxxii.

<sup>34</sup> New York Med. Record, 1872, vol. vii, p. 433.

<sup>35</sup> Prov. Med. Jour. and Retros. of Med. Sci., 1884, vol. ix.

<sup>36</sup> New York Med. Jour. and Rec., 1869.

<sup>37</sup> New York Med. Rec., March, 12, 1881.

<sup>38</sup> New York Med. Rec., 1886, p. 696.

<sup>39</sup> Glasgow Hos. Rep., 1898, p. 120.

<sup>40</sup> Arch. f. path. Anat., 1883, p. 558.

<sup>41</sup> Jour. Amer. Med. Assoc., 1884.

<sup>42</sup> Glasgow Med. Jour., February, 1898.

and Edington reported 4, Moore 1, with unilateral aplasia of the genitals. He believed that males were affected more commonly than females in the ratio of 2 to 1. Edington<sup>43</sup> reported another, and Glazebrook<sup>44</sup> one in a woman aged thirty years, in conjunction with atrophic adrenal. If we allow 240 cases up to the appearance of Ballowitz's paper, then at least 15 more must be added, making a total of at least 255.

In reference to autopsies, Brown found 3 cases in 12,000, Morris<sup>45</sup> 2 in 8068, Sanzalli<sup>46</sup> 3 in 5348, Menzies<sup>47</sup> 2 in 1790, Rootes<sup>48</sup> 1 in 600, and Ballowitz 1 in 617.

In considering the condition in animals, the following has been found: Botalli<sup>49</sup> and J. Van Horn found a single kidney in a dog, while Stoss<sup>50</sup> found the right kidney and ureter absent in a sheep; Newmann<sup>51</sup> noted the same in a horse, and Matthias<sup>52</sup> in a pig. Reterer<sup>53</sup> and Rogers found an absence of the right kidney and ureter, complicated with genital defects, in a rabbit; the right ovary was present, but the corresponding uterus and vagina were absent, while the tube ended in a nodular swelling. Harrison<sup>54</sup> found a rabbit in which the left kidney was absent, the vagina rudimentary, and the uterus and vagina entirely wanting; the ovaries, however, were present. Sutton<sup>55</sup> states that this malformation occurs in the horse, sheep, pig, and hen, while a student of Brown<sup>56</sup> found the defect in a pigeon. According to Marek,<sup>57</sup> congenital aplasia in animals is not rare. Prettnner found at the abattoir that in 15,000 animals killed, two pigs showed agenesis of the kidney, one right and one left, and one steer exhibited the same condition.

I desire to add another case that occurred in a cat. The organs shown in the accompanying illustration were brought to me by a student who had dissected the cat. As can be seen, there is entire absence of the kidney, ureter, and genital tract of the same side. No trace of a ureteral orifice could be detected in the bladder, nor was there a stump of a ureter. In the genital system the narrow vagina leads into a left uterus only. As to the presence of both ovaries, I cannot say, as the student had not noted those structures. As the ovaries are so rarely absent, it is presumed that both were present. The specimen was mounted in special gelatin, as described by Coplin,<sup>58</sup> and is still as good as when prepared in 1903.

<sup>43</sup> Lond. Jour. of Anat. and Physiol., 1903 04.

<sup>44</sup> New York Med. Jour., 1905, p. 174.

<sup>45</sup> Surgical Dislocations of the Kidney, London, 1885.

<sup>46</sup> Cited by Ballowitz, 22.

<sup>47</sup> Jour. Anat. and Physiol., 1887, vol. xxi.

<sup>48</sup> Lancet, 1866, vol. ii, p. 251.

<sup>49</sup> Quoted by Ballowitz.

<sup>50</sup> Deut. Zeit. f. Tiermed. und vergl. Path., 1886, vol. xii, 284.

<sup>51</sup> Glas. Hos. Rep., 1898-99, p. 131.

<sup>52</sup> Quoted by Brown, 21.

<sup>53</sup> Comp. Rend. de Biol., 1893, Ser. 9, Tome v.

<sup>54</sup> Jour. Anat. and Physiol., 1893-94, vol. xxviii, p. 401.

<sup>55</sup> Cited by Brown, 55.

<sup>56</sup> Jour. Anat. and Physiol., 1893-94, vol. xxviii, p. 194.

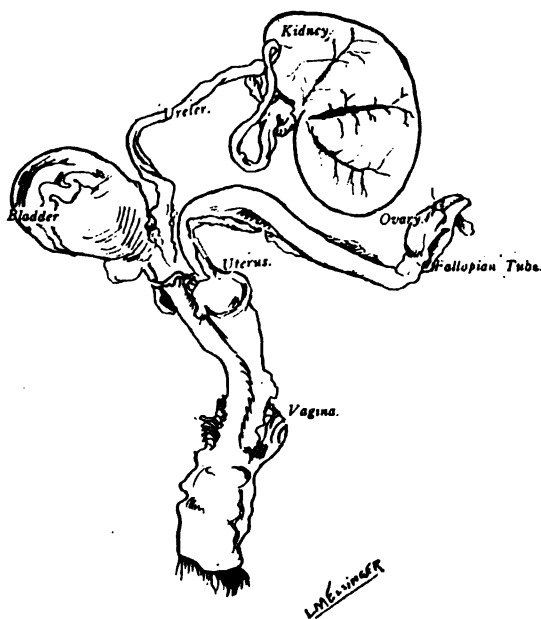
<sup>57</sup> Deut. Tier. Woch., Hanover, 1905, vol. xiii.

<sup>58</sup> Jour. Amer. Med. Assoc., August 13, 1905.

In examining cases in which the genital defects are mentioned, the table on p. 116 has been prepared.

In the male we find the vas, seminal vesicles, and the ejacutatory duct most commonly affected, while the testicle seldom shows changes. No case shows complete absence of the internal genitals, including the testicle. In the female the uterus is most commonly affected, while the ovary is rarely missing.

It might be of some interest to consider the embryology of the urogenital system, with the idea of throwing some light on these malformations and the development of the Muellerian duct.



Urogenital system described in the text.

In considering the embryology we must describe the origin of the pronephros, mesonephros, and duct, and the duct of Mueller. In the development of this system the earliest organ to appear is the pronephros. This consists of a longitudinal tubule developed from the mesoderm, opening caudally into the cloaca, and a few transverse tubules at the cephalad end of the duct. The cephalad extremity opens into the abdominal cavity by means of a trumpet-shaped expansion. This pronephros, however, functionates only in the larval stages of amphibians, and gives way to the Wolffian body, or mesonephros. This consists of transverse tubules that connect with the pronephric duct, and the latter then becomes known as the mesonephric, or Wolffian duct. In the lower vertebrates

TABLE SHOWING CONGENITAL DEFECTS OF THE GENITAL AND URINARY SYSTEMS.

Author	Case No.	Sex	Vas	Vesicles	Ejac. duct	Testicle	Tubes	Uterus	Vagina	Ovary	Remarks
Mosler . . . .	2	Male	A	—	—	$\frac{1}{2}$ A	....	....	....	....	Representing 2 cases
Beumer . . . .	11	"	—	—	—	Small	....	....	....	....	
	4	Male	A	A	—	A	....	....	....	....	
	12	"	—	—	—	Rudimentary uterus and vagina	....	....	....	....	
	14	"	A	—	—	....	....	....	....	....	
	29	"	—	—	—	....	....	....	....	....	
	48	"	Slight	Slight	—	....	....	....	....	....	
	35	Female	..	....	..	....	....	$\frac{1}{2}$ A	$\frac{1}{2}$ A and blind	Small	
	36	"	..	....	..	....	....	Bicornate	$\frac{1}{2}$ vagina duplex	....	
	37	"	..	....	..	....	....	Duplex	Vagina simplex	....	
	39	"	..	....	..	....	....	Left horn absent	—	....	
	41	"	..	....	..	....	....	Left horn absent	—	....	
	42	"	..	....	..	....	....	Unicornis	—	....	
	43	"	..	....	..	....	....	Bicornis	—	....	
	45	"	..	....	..	....	....	Unicornis	—	....	
Ballowitz . . . .		Male	A	A in 3	—	....	....	....	....	....	Representing 13 cases
		"	A	Atrophic in 2	—	....	....	....	....	....	
		"	—	—	A in 3	....	....	....	....	....	
		"	—	—	A in 4	....	....	....	....	....	
		Female	..	....	..	A in 2	....	Bicornate in 18 (8 l. and 10 r.)	....	....	Representing 41 males
						Small and atrophic in 8	....	Double cavity in 10	....	....	
						....	....	....	....	....	
						....	Absent in 5	Absent in 5	Double in 2	Absent in 3	
						....	Absent in 3	Absent in 1	Absent in 1	Absent in 3	Representing 28 females
						....	....	Bicornis	A	....	
						....	....	A	....	....	
						....	A	Unicornis	—	Absent	Total males 49
						....	....	....	....	....	Total females 41

A = absent. — = nothing stated in regard to those organs.

(selachians), Semper, Balfour, Hoffman, and Rabl believe that the Muellerian duct is derived from the mesonephric duct by segmentation, or longitudinal splitting of this duct; the trumpet-shaped upper extremity of the mesonephric duct falls to the Muellerian tube in this division. This occurs also in amphibians, according to Hoffmann and Furbringer, with the exception that the fimbriated end is derived especially from the abdominal mesothelium by a thickening and latter invagination of the mesothelial cells; this part finally gains connection with that derived from the mesonephric duct. Semon, however, finds that this does not occur in all amphibians. In reptiles, birds, and mammals the origin of the Muellerian duct is in dispute. Waldeyer, Braun, Gasser, Janhosik, Mihalkovics, and others do not believe in the segmentation, or splitting, of the Wolffian duct as the origin of the Muellerian tube. This seems corroborated by Wiedersheim, Hoffmann, and Nagel, as they find that it appears later than the pronephric duct and is composed of a solid cylinder of cells with a trumpet-shaped invagination of the mesothelium of the body cavity, this latter becoming the ostium abdominale of the oviduct.

The mesonephric duct opens caudally into the cloaca. From this end the metanephric evagination, which becomes the permanent kidney, ureter, and pelvis, appears. In addition to this, in the male this duct gives rise to the body and globus minor of the epididymis, the vas, seminal vesicles, and ejaculatory duct, but nothing of importance in the female. In the female the ducts of Mueller fuse for over half of their length, and ultimately form the uterus and vagina, while the unfused portions constitute the oviducts.

If we examine the table, we note that the genitals are defective in 90, 49 males and 41 females, and one doubtful case of Moore's. In all there are about 255 cases of absence of the kidney and, of these, 100 show decided defects in the genitalia, over one-half of which occur in males. The parts affected are as follows: The vas practically absent in 22, the vesicles in 20, the ejaculatory duct in only 9, and the testicles in 15. In the female we find the uterus entirely absent or bicornate in 12, the vagina absent or reduced one-half in only 5, and the oviducts missing in 9, while the ovary was absent in but 4.

Absence of the kidney may be due to the following causes: (1) Failure of the metanephric evagination to appear, even though the mesonephric duct and body be perfect; (2) appearance and early retrogression of the metanephric evagination; (3) failure of the pronephros, and therefore also the mesonephros, to appear.

In the first instance the absence of the kidney in the male would naturally be attended by few if any genital defects, and these would be coincidental and not sequential. In the second instance the resultant conditions would be the same. In the third all such cases would be attended by absence of the kidney, ureter, efferent ductular

system of the testicle, vas, and vesicle on the affected side. From the irregularity of the occurrence of the genital defects, the absence of the kidney seems to be due entirely to the first or second cause; the genital defects then occur secondarily, and not as a direct result of absence of the kidney; that is, they are merely coincidental. Another reason for taking this view is the fact that in most of the cases of absent kidney and ureter the vessels also were absent or rudimentary, pointing more to the first or second cause.

In the female in the first or second cause there would be no genital defects, whether we assume that the Muellerian ducts are derived from the mesonephric duct or independent; such defects would then be merely coincidental. In the third cause, if the Muellerian ducts were derived from mesonephros partially or entirely, then as a result of its absence the entire internal genitals should be practically absent. In fact, that has not occurred in any case. In reality, the uterus was absent or bicornate in but one-third of the cases. The facts as found in the adult body seem to indicate that the Muellerian ducts have an independent origin and are not derived from the mesonephric duct by segmentation, at least not in the higher vertebrates.

## REVIEWS.

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**SYPHILIS: A TREATISE FOR PRACTITIONERS.** By EDWARD L. KEYES, JR., M.D. Pp. 577; 69 illustrations; 9 plates. New York and London: D. Appleton & Co., 1908.

THE "foreword" to this book, written by the father of the author, states that "the facts upon which the volume rests are the classified cases" from private office books kept during forty years, other and similar work by the author himself, and "gleanings" from Dr. Van Buren's case books. Dr. Keyes, the elder, speaks of himself as "the godfather of many of the generalizations advanced," but adds later that they "corroborate quite uniformly similar generalizations of other authors often based upon statistics numerically superior." This would appear to be correct, and, so far as the views advanced are those generally accepted by syphilographers, there is no occasion to review them in detail. As a rule, they are well and correctly stated.

Even in a scientific field so thoroughly cultivated as that of syphilis there must, however, be outcroppings of new beliefs or new theories, which will seem to one observer firmly rooted and valuable, to another ephemeral and useless, or harmful; and there are many more that at any given time will be regarded by some as having demonstrated their value, but by others are thought still to be on trial. Here and there in this treatise are to be found teachings that seem to the reviewer too dogmatic for the present state of our knowledge, and generalizations that are not yet justified by the facts at our command.

It is stated that the advocate of the regulation of prostitution can show, as a result of regulation, "no marked decrease in the incidence of venereal disease." This is too sweeping. Diminution of such diseases has repeatedly followed what the author calls "reglementation," and, indeed, in a foot-note two pages farther on, he says: "The incidence of syphilis is highest in the English army (75 per mille per annum). Then follow the United States (33.98), Austria (19.2), Russia (12.8), France (6.7), Holland (4.9), Bavaria (4.3), Prussia (4.0). The prudish Anglo-Saxon refusal to countenance protective measures for the health of the army here shows its results." This does not refer exclusively to the control of prostitution, but it, of necessity, includes it.

The assertion that the mother of a syphilitic child "almost invariably ultimately breaks out with tertiary syphilis," and the statement that "all syphilis is relapsing syphilis," are not in accord with the observed facts. Such a mother may develop tertiaries; any case of syphilis may relapse. These are facts, and, indeed, the context shows that, in the latter instance, this is what was meant; but accuracy has been sacrificed to terseness and to a certain striving for epigrammatic statement noticeable throughout, which tends to make agreeable reading but unsound teaching.

We believe, with the author, that the "spirocheta of Schaudinn is either the cause of syphilis or one phase in the life cycle of some microörganism which is the cause of syphilis," but we would not yet venture to say that it "seems certain," nor can certainty be asserted until the organism has been successfully cultivated. The results of experimental inoculation upon the anthropoid and other monkeys are now adding constantly to our knowledge of the disease, but they do not yet justify the absolutely unqualified announcement—italized—that "syphilitic secretions cease to be infectious after twelve to twenty-four hours, and much sooner (at most six hours) when dry." This may be true, but until we *know* that it is true the practical possibilities of evil from accepting and acting upon it should not be forgotten.

Even more important is it to remember the present lack of demonstrative proof of the following statement: "The only personal prophylaxis against syphilitic infection lies not in cauterization or excision, but in inunction with a strong mercurial ointment within one hour of inoculation." The author adds that "perhaps as late as six hours the remedy might still be efficacious." It is harmless, and may well be tried, but dependence on its efficacy at any time might certainly lead to disastrous consequences. It is to be feared that extended trial will show that (as in the local treatment of chancre and other open lesions) mercury may have some slight local effect, but that—as the author says elsewhere—systemic treatment must be employed to obtain "real results." He adds: "Experiment has proved that inunction or injection of mercury encourages healing of adjacent syphilitic lesions; but clinically this local action is of little importance."

It is impressive to say, "Nothing is certain in syphilis except its uncertainty," but, as a matter of fact, it is one of the most orderly of the infectious diseases from its incubation to the termination of the period of clinical contagion.

It is open to reasonable doubt that "syphilis in woman, though it ceases to be transmissible by contact quite as early as in man, may continue transmissible by heredity for an indefinite number of years." At any rate, the statement should be more closely coupled with the undoubted rule—accurately formulated a few pages later—that "the probability of syphilitic heredity, like the probability



of contact infection (in matrimony), is overwhelming in the first year of the disease, great in the second and third years, slight in the fourth and fifth years, and negligible thereafter."

The chapter on the treatment of syphilis, and that on the physiological and toxic effects of mercury, deserve almost unreserved commendation. In that on the administration of the drug, the advantages of insoluble injections appear to the reviewer to be overstated and the dangers and disadvantages correspondingly minimized. Embolism, of which a number of fatal cases—not "one or two"—have been reported, is scarcely to be called a "petty inconvenience," even in comparison with the benefits sometimes unquestionably to be derived from the injection method. Nor do inunction and internal administration, in the opinion of many syphilographers, rank in efficacy below fumigation, as is asserted by the author.

It is true that the characteristic early syphilitic adenitis may not occur so that the nodes are palpable, but such cases are so rare that the statement that if the nodes are not enlarged "the evidence has no value" would be most misleading if accepted as a diagnostic rule. The chapters on regional syphilis are valuable summaries of our knowledge of the subject, those on special organs or systems having been reviewed for the author by various specialists, to whom due acknowledgment has been made. No mention of mammary syphilis was found by the reviewer, except in relation to chancre of the nipple.

Here and there a little carelessness in writing—or in proofreading—is manifest, *e. g.*, "among the literature;" "this . . . spread John Hunter's name," "a host of practical queries . . . are constantly clamoring for answer;" and one remarkable paragraph, which reads: "Thus Fournier narrates cases of infection transmitted to a child by its uncle, who blew his syphilitic child; and this exception is fully compensated for by 3 other case in which a kindly lady bound up the scratched knee of a little child with her handkerchief saturated with saliva!" The "kindly lady" reminds one of the sort of redundancy recently exemplified by a critic of English, who says that it is as though one should breathlessly announce: "A gentleman of much personal refinement has just fallen from the third story window," or "A lady with a fine command of modern languages is struggling for her life in the river."

To emphasize such criticism would, however, be not only ill-natured, but unfair to a book which shows industry, and experience on the part of its author. As the most recent addition to the treatises on syphilis, it is deserving of careful reading, and, as a rule, in its broader teachings may safely and advantageously be followed by the general practitioner.

J. W. W.

MODERN SURGERY. BY JOHN CHALMERS DA COSTA, M.D.,  
Professor of the Principles of Surgery and of Clinical Surgery  
in the Jefferson Medical College, Philadelphia. Fifth edition;  
pp. 1283; 872 illustrations. Philadelphia and London: W. B.  
Saunders Co., 1907.

THIS volume is the fifth edition of Da Costa's *Surgery*, and a glance at the copyright page shows that in addition the book has been reprinted many times since its original appearance in 1894. With such a history, praise seems superfluous and criticism needless. Many of the sections have been corrected and much new matter has been introduced, particularly along the lines of improved technique. The encyclopedic character of the book is impressed upon one before many pages have been turned, and the author is particularly to be commended for the frequent interpellation of references, which not only serve to show the practising physician where such information was acquired, but also tends to encourage the undergraduate student to read further than his text-book. Almost everything relating to surgery, whether in pathology, diagnosis, or operative technique, seems to be included, and it is this jumbling of the good with the bad, the modern with the old, that offers a point for criticism. Many methods are mentioned and some are described in detail, only to have added to them at the end that the author does not use them in his own practice, or that they have been generally discarded by the profession. The earlier chapters devoted to surgical pathology are generally excellent, although most of the illustrations are old and give but little idea of the lesions they are meant to illustrate. The chapters upon the treatment of hemorrhage, upon tumors, fractures, brain injuries and tumors, and spinal cord injuries, are particularly good. In the treatment of the latter the advocacy of early operation in all cases in which the symptoms are significant is based on sound reasoning. The surgery of the respiratory and the genito-urinary organs is well balanced and generally excellent. In discussing the treatment of acute peritonitis the author gives a splendid presentation of modern methods, in particular condemning flushing of the abdominal cavity. The Fowler position and Murphy's method of proctolysis are advocated. The entire section devoted to the various diseases and injuries of the abdomen is most interesting and clear cut. The chapter upon the thyroid gland is also well arranged; the author prefers local anesthesia for thyroidectomy and makes no mention of the parathyroids in relation to tetany.

In the chapter upon inflammatory diseases of bone, caries, necrosis, osteitis, and chronic osteomyelitis are not discussed with the usual clearness characteristic of the book. As the author states, "the term caries is seldom used today except loosely," and the same might have been said of necrosis. Descriptions of the sequential lesions of osteoperiostitis or of osteomyelitis, with appropriate

treatment of caries or necrosis as they occur, would seem the preferable way of teaching, instead of placing the latter terms in heavy type as separate diseases. Bier's method of passive congestion is barely mentioned, and that only in tuberculosis, in which, except in early cases, it has its most limited field. The method of treatment recommended for what is called "osteo-arthritis" is inadequate, no distinction being made between the atrophic and the hypertrophic varieties. Objection might also be taken to the statement that removal of the Gasserian ganglion is dangerous, bloody, and difficult; if the patient is operated on in the sitting position, and if the skull opening is made posterior to that of the Hartley-Krause method, the objections disappear, and a mortality of 10 per cent. is not particularly objectionable when we consider the life of torture which such patients must lead. The pathology of cysts and tumors of the mammary gland, as given, is very confusing, and a scirrhus cancer of the breast is not "almost as hard as stone."

These few criticisms are not made with a view of minimizing the value of this book, because, as it stands, it is probably the best one volume text-book on surgery that we have. The different sections are particularly well balanced, lengthy and complete descriptions being given of important subjects and diseases especially common in surgical practice, and yet the rare and unimportant lesions are adequately described. The 1200 pages represent an immense amount of labor in condensation, and while the omissions mentioned have been noted in glancing through the book, yet a similar list could be found in any other text-book. The index is very complete.

G. P. M.

**SURGICAL EMERGENCIES.** By PERCY SARGENT, M.A., M.B., B.C. (Cantab.), F.R.C.S., Surgeon to Out-patients, St. Thomas' Hospital, London. Pp. 256. London: Henry Frowde, Oxford University Press; Hodder & Stoughton, 1907.

THIS book was written for those who "require in any emergency, not academic discussions concerning the relative value of different methods, but explicit directions as to some definite line of treatment, which, if not always the best, has, at least, the merit of having been found by experience to be sufficiently good." With this gentle apology in his preface, the author introduces us to an eminently practical work, in which he succinctly describes the symptoms and treatment of such surgical emergencies as hemorrhage, burns, fractures, acute infective diseases (including those of the abdomen); injuries of the abdomen, strangulated hernia, respiratory obstruction; as well as emergencies connected with the urinary system;

injuries of the neck, chest, nervous system, ear, and eye. It is a volume which will prove of interest to every active surgeon, and which, better than any handbook with which we are acquainted, will fill the want of resident physicians on duty in the receiving wards of large hospitals.

There can be few criticisms of the treatment recommended; it is, with few exceptions, that which is approved by judicious surgeons the world over as expedient and safe. Yet not to even mention elevation of the limb to control hemorrhage seems an unpardonable omission; and we think the routine use of general anesthesia in the reduction of fractures is needlessly commended. The treatment advised for tetanus seems scarcely up to date, and we are surprised to be told that the majority of surgeons have abandoned intubation in diphtheria in favor of tracheotomy. Nor can we agree with the recommendation to sponge away all peritoneal exudate in cases of diffuse peritonitis, and to administer calomel and salines as soon as the patient is able to swallow.

On the whole, the book admirably fulfils its purpose, and the points adversely criticised have been noted merely because we had thought they were no longer mere matters of opinion, but of fact.

A. P. C. A.

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ATLAS AND EPITOME OF DISEASES OF CHILDREN. By DR. R. HECKER and DR. J. TRUMPP, of the University of Munich. Authorized translation from the German. Edited by ISAAC A. ABT, M.D., Assistant Professor of Diseases of Children in the Rush Medical College, Chicago. 48 colored plates and 147 black and white illustrations. Philadelphia and London: W. B. Saunders Co., 1907.

THIS latest volume of the well-known *Lehmann's Medical Hand-Atlases* is a worthy companion to the various volumes already translated. Like them it is especially noteworthy for the profusion and beauty of its illustrations, the large number of colored lithographs presenting most striking and lifelike reproductions of many eruptive diseases, those picturing the clinical appearances of the exanthemata being especially successful.

While the volume is essentially a picture-book, the text is by no means a mere descriptive narrative to fit the illustrations, and its value in the original has been greatly enhanced by Dr. Abt's judicious editorial annotations. Numerous changes in the text have been made by the American editor in the sections on therapeutics, necessitated by the differences in treatment obtaining in this country, and by the fact that many of the special food preparations and various forms of apparatus used in Germany are either unknown or unobtainable here.

It is not expected that the hand atlas should take the place of larger and more comprehensive text-books on diseases of children. To the most important subject of artificial feeding, for instance, only four pages are devoted, and nearly two pages of this allowance are given to an enumeration of patent foods and the special milk products which are so generally used in Germany. As a supplement, however, to clinical study, within the reach of every student, the present volume should be a welcome addition to any working library.

T. S. W.

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MOSQUITO LIFE. By EVELYN GROESBEECK MITCHELL, A.B., M.S.  
Pp. 281. New York: G. P. Putnam's Sons, 1907.

THE American people, especially those living in our larger cities, have shown distinct apathy in regard to great hygienic problems, in spite of thousands of preventable deaths occurring yearly from communicable diseases. There seems to be but little desire to expend money to wipe out endemic diseases, such as typhoid fever and tuberculosis. Any book, therefore, that may arouse public interest in preventive medicine, and that shows reasons for and means of checking disease has, in this country, a distinct value, even though the story may not be new, and even though it serves merely as a reminder of well-known facts.

The volume by Evelyn Groesbeeck Mitchell falls into this class of books. Mosquitoes are discussed from various points of view. "How and where they breed, how they bite, how they transmit disease, how long and on what they live, how they may be identified in their various stages, and finally, but not the least important, how they may be locally controlled." The book contains on all these subjects many original observations made by the author and by Dr. James William Dupree, a life-long student of the subject. The death of Dr. Dupree prevented him from bringing forth his own observations, but the author has done this, together with much praise and esteem for the man and his work.

The book is written in a semi-technical style, and requires no extensive zoölogical training for its successful use in the field and in the laboratory as a means of identification of the various species and for much information as to their habits. The keys for identification are especially good features of the book. The literary style is somewhat unfortunate. It neither has the seriousness of a thoughtful scientific treatise, nor does it contain enough true literary merit to make it a book to which one would likely turn for diversion. The author includes a number of trivial things that annoy when the book is put to serious scientific use.

The chapters on malaria and on yellow fever and other diseases

are largely taken from the notes of Dupree. They contain nothing that is especially new to medical science. Some of the statements are not in accord with the ideas usually held by the profession, and one or two rather obvious errors can be found. However, the book should be of distinct value as a guide for determining the various species and as an authority on their habits and their dangers, information that should be sought for in all mosquito-infested districts before attempts at control of the pests can be intelligently undertaken.

G. C. R.

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INSANITY AND ALLIED NEUROSES. A PRACTICAL AND CLINICAL MANUAL. By GEORGE H. SAVAGE, M.D., F.R.C.P., with the assistance of EDWIN GOODALL, M.D. (Lond.), B.S., F.R.C.P. New and enlarged edition; 6 colored plates and 45 illustrations in the text. Chicago: W. T. Keener & Co., 1907.

THE fourth edition of a manual on this subject does not deserve an extensive review. This edition does not differ essentially, except in the matter of the illustrations, from the previous third edition. With 45 illustrative cuts in the text and 6 colored plates, the book may be considered to be fully illustrated; the new cuts have added to the value of the work. The only criticism to be advanced against this book is the fault of ultra conservatism. Practically none of the newer ideas concerning the insanities of adolescence are included. The same conservatism is seen in the general classification of the insanities. The chapter on the commitment of the insane follows the British Law, and, of course, will be of relatively little value to the American student and practitioner. The book can be recommended as a good, conservative presentation of the subject of insanity, for students and practitioners.

D. J. McC.

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A TEXT-BOOK OF PRACTICAL GYNECOLOGY. By D. TOD GILLIAM, M.D., Emeritus Professor of Gynecology in Sterling (Ohio) Medical College. Second Edition; pp. 621; 364 illustrations. Philadelphia: F. A. Davis Co., 1907.

As stated in the preface to the earlier editions, Dr. Gilliam's book has been prepared to meet the demands of the student and the general practitioner. This it does in a very satisfactory manner. In this second edition the book has been brought well up to date by the inclusion of new material. The whole field of gynecology proper is embraced, and, in addition, chapters are included upon diseases of the rectum and of the kidneys. The operation devised by the author, and known by his name, for the correction of retrodisplace-

ments of the uterus, is well and fully described. It has been tried and found successful by the technique of the author, and also by many other surgeons, with slight modifications, and is, we believe, the best of the round ligament operations. We would suggest, however, that the description of the operation of ventrosuspension be altered in the next edition of the book, since, for those who are still advocates of this form of intervention, the present description is not adequate. We refer to the statement that as a means of uterine support the peritoneum is alone depended upon, to the exclusion of small portions of the recti muscles. We note with pleasure the general definiteness of statement throughout the book, as, for instance, the author's absolutism in his statement that it would be well if all women between the ages of thirty-five and sixty years could be looked after by a competent gynecologist, and, when considering the use of the uterine curette, that "it is a question, indeed, if the curette used postpartum has not killed more than it has saved." The profession in general needs clear, concise, and, above all, dogmatic statements such as these. W. R. N.

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A HISTORY OF NURSING. THE EVOLUTION OF THE METHODS OF CARE FOR THE SICK FROM THE EARLIEST TIMES TO THE FOUNDATION OF THE FIRST ENGLISH AND AMERICAN TRAINING SCHOOLS FOR NURSES. By M. ADELAIDE NUTTING, R.N., Superintendent of Nurses in the John Hopkins Hospital, Baltimore, and LAVINIA L. DOCK, R.N., Secretary of the American Federation of Nurses and of the International Council of Nurses. Vol. I, pp. 549, Vol. II, pp. 461; illustrated. New York and London: G. P. Putnam's Sons, 1907.

THE two volumes prepared by Miss Nutting and Miss Dock comprise an exceedingly interesting account of nursing from the earliest available records to the time of the development of modern nursing. The work is divided into three parts, of which the first relates to the pre-Christian period and consists of a description of the care of the sick of primitive man and in India, Ceylon, Egypt, Babylon, Assyria, among the Jews, and in Greece and Rome. Part II comprises the period from the first to the close of the eighteenth century; here is well described the leading part in nursing taken by woman with the advent of Christianity, the relationship of the Roman matrons to the early hospitals, the rise, development, and progress of religious nursing orders, and the later development of nursing apart from the influences of the church. Part III deals with the period from the close of the eighteenth century to the development of modern nursing. Much that is of interest in this period naturally centres about

Florence Nightingale, and it is very well told. There is a chapter on the development of nursing in America, and another on a trio of early training schools—that of Bellevue Hospital in New York, that of the Massachusetts General Hospital in Boston, and the Connecticut Training School in New Haven. Throughout both volumes there is ample evidence of an unusual amount of investigation, of the searching of old records, and of the sifting of much data. The result is a credit to the authors and a noteworthy contribution to the literature of nursing; it must prove a source not only of information, but also of delight to all, physician, nurse, and layman, who may have the good fortune to read it.

A. K.

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**THE CLIMATIC TREATMENT OF CHILDREN.** By FREDERICK L. WACHENHEIM, M.D., Chief of Clinic, Children's Department, Mount Sinai Hospital Dispensary, New York. Pp. 400; 5 charts. New York: Rebman Company, 1907.

THE common sense which chooses the apparently unoriginal but none the less useful method of "tempering the wind to the shorn lamb" is worth noting in this day of fads; wherefore this book, while intended primarily as a reference book for the pediatricist, should prove agreeable and wholesome reading to overzealous patients or those interested in the care of delicate children. The author has given considerable space to the climatic conditions in North America, with special reference to the value as health resorts of the different parts of the country, and for those patients who must be treated at home there is much good counsel.

R. M. G.

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**DISEASES OF THE SKIN.** By HENRY W. STELWAGON, M.D., Ph.D., Professor of Dermatology in the Jefferson Medical College, Philadelphia. Fifth edition; pp. 1150; 301 illustrations. Philadelphia and London: W. B. Saunders Co., 1907.

THE fifth edition of Stelwagon's *Diseases of the Skin* brings to our attention a book that has been five times revised in as many years—than which there can scarcely be better evidence of conspicuous merit. In the present edition the noteworthy changes are in connection with diseases of warm climates, such as frambœsia, oriental sore, verruga peruana, tinea imbricata, dhobie itch, and uncinarial dermatitis, which have been entirely rewritten or materially altered. As a text-book and work of reference the volume is probably unsurpassed, and it will doubtless continue to enjoy the favor of the profession.

A. K.



# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**The Relation of the Parathyroids to Calcium Metabolism and the Nature of Tetany.**—W. G. MACCALLUM and C. VOEGTLIN (*Johns Hopkins Hospital Bulletin*, 1908, xix, 91) note that clinical studies of such conditions as rickets, osteomalacia, etc., have suggested the possibility that tetany might stand in some relation to disturbances of the calcium metabolism; also that calcium counteracts the effect of other salts which produce muscular twitching, and moreover that in animals, after parathyroidectomy, which are kept on an abundant milk diet rich in calcium, the tetany is either very mild or absent. This led MacCallum and Voegtlin to study the calcium metabolism of animals in which tetany is produced by parathyroidectomy, and the relations of various salts, especially those of calcium to the tetany thus produced. They conclude that all the violent symptoms caused by parathyroidectomy may be almost instantly cured by the intravenous injection of a solution of a calcium salt (either 5 per cent. of the acetate or lactate of calcium). Subcutaneous injection or taking the salt by the mouth are as effective but act more slowly. This beneficial action lasts for about twenty-four hours, when tetany may reappear; it disappears however, with the repetition of calcium therapy. Potassium salts have an opposite effect and aggravate the symptoms of tetany. These accentuated symptoms may be relieved by the calcium salts, but larger doses are required in order to overcome the added potassium effects. Magnesium has a similarly beneficial effect, but its toxic anesthetic action obscures the results.

This article is a preliminary note, and more work is being carried on along these lines by MacCallum and Voegtlin, which will appear later. That so far done indicates, however, that there is a deficiency in the calcium

content of the blood of dogs during tetany, and the excreta show an increased calcium output. Thus, apparently, the parathyroids control in some way the calcium metabolism, so that upon their removal a rapid excretion, possibly associated with inadequate absorption and assimilation, deprives the tissues of calcium salts. Thus, the administration of these calcium salts may have some therapeutic importance, not only in post-operative tetany, but also in those forms occurring spontaneously, as in children and in some infectious diseases or in pregnancy and lactation. "If further study confirms the accuracy of these observations it may be possible to compare the condition with that in pancreatic diabetes, in which the loss of control of the carbohydrate metabolism by the destruction of the Islands of Langerhans allows an abnormal carbohydrate excretion, and tetany might accordingly in that case be spoken of as a *diabetes calcareus*."

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**Masked Pneumothorax.** C. SABOURIN (*Rev. de méd.*, 1908, xxviii, 89) gives this name to those cases of pneumothorax in which, although the symptoms and the condition of the patient point to the trouble, yet physical signs are either absent or in abeyance for a while. This may also be the case in certain central pneumonias and interlobar pleurisies, and in some instances of tuberculous cavities in which, at times, the usual physical signs are wanting. These changes from the usual pictures are brought out by the depth of the lesion. In pneumothorax, if the opening be into the mediastinum, interlobar, or toward the diaphragm, and particularly in those cases in which the area becomes more or less encysted, the difficulties of diagnosis are much greater than ordinarily. Sabourin reports four cases of tuberculosis that presented suddenly the symptoms of pneumothorax, pleuritic pain, dyspnoea, and signs of compression, displacement of the mediastinal organs and diaphragm without any auscultatory or percutatory phenomena. These signs were in abeyance for from three to six days. A fifth case of the same character is described in which there were no signs of pneumothorax before death, yet at the postmortem they were evident. In these cases the many pleuritic adhesions helped undoubtedly to mask the condition.

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**Heart Disease and Pregnancy.**—L. POULIOT (*Arch. gén. de méd.*, 1908, lxxxviii, 65). Since 1869, when Professor Peter, after seeing a sudden death in pregnancy due to heart disease, enunciated the following so-called law, that in such conditions "girls should not marry, wives should not have children, and mothers should not nurse their children," there has been more or less discussion of the subject, some advocating these stringent measures, others more lenient except in the presence of grave cardiac lesions. These views Pouliot has carefully considered, and after a study of the subject does not think that all forms of cardiac disease forbid pregnancy. Mitral stenosis is the most serious condition, especially as acute pulmonary complications are apt to set in, oedema being the most serious. The myocardial conditions, when at all advanced, are also very serious, especially when there is marked asystole, the mortality in these cases being very high—46 per cent. in 555 cases. As regards treatment in these conditions the rapidity

of the symptoms leading up to pulmonary œdema is often so great that venesection is the best treatment. This should be followed later by cardiac stimulants and the interruption of pregnancy or the ending of labor as soon as possible. Pouliot notes, however, the great frequency of perfectly normal pregnancies and deliveries of women suffering from the various heart diseases; this is especially brought out in routine hospital examinations in which the cardiac lesions are discovered without specially suggestive symptoms. Pouliot, therefore, concludes that with the exception of the graver conditions noted above, ordinary cardiac lesions need not be a bar to pregnancy and successful labor.

**Hemophilia.**—MARCEL LABBÉ (*Rev. de méd.*, 1908, xxviii, 103) considers the pathogenesis and treatment of this interesting condition. As regards its etiology, he groups the condition under four headings and summarizes briefly the different views in literature as to whether its cause lies in the heart or in the circulatory system, whether it is of nervous origin or due to some inherent trouble in the blood. This latter view he discusses most thoroughly. Of especial interest, however, is the treatment of the disease. Labbé goes over various drugs and methods and comments upon their value. The most recent and successful method of treatment is the injection of fresh normal blood as advocated by P. E. Weil, either from the horse, rabbit, or human blood. Beef serum must not be used, as it is apt to set up a febrile reaction. In case of necessity a horse's antidiphtheritic serum may be used. The dose, if given intravenously, is 10 to 20 c.c.; if given subcutaneously, this should be doubled. Serum must be fresh; that is, not older than fifteen days. After injection the coagulability of the blood is greatly increased, and this effect lasts for some weeks, although it is at its height within the first two to three days. The good effect of the serum is more evident in those cases in which the cause lies in the blood plasma rather than in the permeability of the vessel wall. In other cases the condition is benefited, but not as much. The injection may be repeated when necessary, with the same effects as in a primary inoculation. By means, then, of this serum which may be injected before surgical operations, work of this character may be done on hemophiliacs without an alarming hemorrhage. It never could be done before. Gauze soaked with the serum is of great use in minor surgical work, and has proved successful in dental surgery and in severe epistaxis.

**Experimental Studies on Posthemorrhagic Anemias and Their Relation to Aplastic Anemia.**—BLUMENTHAL and MORAWITZ (*Deut. Arch. f. klin. Med.*, 1907, xcii, 25) first review the cases of aplastic anemia reported in the literature, emphasizing the salient clinical and pathological anatomical features of the disease. As hemorrhage has been a prominent symptom in the history of several cases, they undertook to reproduce in the lower animals by repeated bleedings, histological changes analogous to those occurring in the aplastic anemia of man. Their experiments were carried out upon dogs and rabbits. The dogs were bled daily from a vein, over a considerable period of time; with the rabbits leeches were used to remove the blood. Young animals were found to be suitable for the work because of the rapidity with which their blood is

regenerated after hemorrhage. In older animals, in which the hematopoiesis is less active, the bone marrow showed only slight hyperplasia; this was of the myeloblastic type—the predominating cell being mononuclear and non-granular, nucleated red blood cells; granulocytes were very few in number. In the spleen megalokaryocytes were found, but they saw no evidences of blood formation here. In one instance the spleen contained numerous phagocytes filled with red cells. No signs of blood formation were observed in the liver. The peripheral blood, which was frequently examined, resembled that seen in aplastic anemia in man in the absence of poikilocytosis and the small number of nucleated red blood cells, and differed from it in the presence of basophilic granules and polychromatophilia in the red cells, and in the absence of leukopenia and lymphocytosis. The basophilic granules of the erythrocytes Blumenthal and Morawitz look upon as nuclear in origin; the granules were found in the blood of those animals in which regeneration was most active; they were not found in association with aplastic bone marrow, evidence of their nuclear source.

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**The Diagnosis of Chronic Pentosuria.**—VAS (*Wien. klin. Woch.*, 1908, xxi, 313) reviews the cases of chronic pentosuria and adds two cases of his own. The condition is a perversion of metabolism without characteristic symptoms and is not incompatible with good health. Alimentary pentosuria, which may follow the ingestion of cherries, plums, etc., bears the same relation to chronic pentosuria that alimentary glycosuria bears to diabetes mellitus, and the two conditions must, of course, be sharply differentiated. With the usual orcin and phloroglucin tests employed for the detection of pentoses in the urine, apparently positive results may be obtained from the presence of paired glycuronic acid compounds. Vas has found Bial's modification of the orcin test of value in avoiding this difficulty. (Bial's reagent consists of hydrochloric acid, concentrated 500 c.c., in which is dissolved 1 gm. of orcin; to this solution 20 to 80 drops of 10 per cent. ferric chloride are added). The rarity of chronic pentosuria is shown by the fact that Vas met with but two instances in about two thousand specimens of urine examined for pentoses.

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**Alimentary Lipemia.**—NEISSER AND BRAUNING (*Ztschr. f. exp. Path. u. Ther.*, 1907, iv, 747) have made a very extensive study of digestive lipemia. A few drops of chyle suffice to render cloudy 100 c.c. of clear blood serum. After each meal rich in fat a fairly strong stream of emulsified fat flows into the blood from the thoracic duct, and the turbidity of the serum which is produced thereby is very readily detected by the unaided eye.

The serum of 96 patients was examined after twelve hours fasting (6 P.M. to 6 A.M.). Of these, 84 had perfectly clear blood serum, while in 11 they found a slight turbidity and in one a marked opacity. The 12 patients with turbid serum suffered from the following diseases: Diabetes, 1; intermittent glycosuria, 2; alcoholism, 4; acute nephritis, 1; adiposity, 1; carcinoma of the liver, 1; 2 had no disease. The very cloudy serum was obtained from a patient suffering from arteriosclerosis and alcoholism. Experimentally they found clear serum in six cats which had been starved forty-eight hours. They therefore conclude

that in man, twelve hours after the last meal, and in fasting cats, the serum is clear except in certain diseases. If a man has eaten a few hours before the blood is taken, the serum is nearly always cloudy. Neisser and Bräuning find, by giving specially chosen meals, that the cloudy serum is obtained only after the patient has eaten food containing fats. They now examined the serum of seventy-one patients following the administration of 100 gm. cream to which 70 gm. fluid butter had been added; turbid serum was met with sixty-seven times, clear serum four times. The patients with clear serum suffered from cirrhosis of the liver (fatty stool), cancer of the liver (fatty stool), cancer of the pancreas (fatty stool), and cancer of the esophagus (shortly before death) respectively. In cats they always found a cloudy serum after a fat meal. Thus, they conclude that the blood serum is always cloudy a few hours after the giving of a meal rich in fat, except when there is interference with the absorption of fats. The microscopic appearance of the blood with turbid serum was striking. Fat droplets of various sizes are seen. The smallest are identical in appearance with hemokonia, and, like the latter, they show well-marked Brownian movement. Using the ultramicroscope, one can see still smaller droplets. If, now, one shakes out a turbid serum obtained after a fat meal with some ether, the serum becomes clear and the hemokonia are no longer to be seen. Allowing the ethereal extract to evaporate, a fatty residue results. Further, if 100 gm. of butter is melted and stained with Sudan III and then given to a cat, the serum taken in the next few hours will show numerous hemokonia stained red. The identity of hemokonia, is, therefore, established. By administering to the patient a fat which does not remain fluid at moderately low temperatures, the degree of the alimentary lipemia may be measured directly. The method is as follows: The patient fasts during the night. At 7 A.M. he is given 100 gm. cream and 30 gm. butter. During the remainder of the day fat-free food must be given. Blood is withdrawn at intervals of a few hours for twelve hours after the test meal. The serum after complete separation is drawn into long, narrow, glass tubes and placed in the refrigerator. In the course of twenty-four to forty-eight hours a "cream" will collect on the surface. The height of this layer, compared to the column of serum, may be used to express the degree of lipemia.

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**Cellular Changes in the Blood-forming Organs.**—MORAWITZ and REHN (*Deut. Arch. f. klin. Med.*, 1907, xcii, 109) have studied the myeloblastic bone marrow obtained by Blumenthal and Morawitz as a result of their work upon aplastic anemia. They distinguish the non-granular cells of the bone marrow (myeloblasts) from the lymphocytes and lymphoblasts solely by the granules in the protoplasm as shown by Altmann's stain. In smears and sections of the spleen and lymph glands one finds a few granules placed about the nucleus in the lymphocytes and lymphoblasts; in the lymphoid cells of the bone marrow (myeloblasts) these granules are completely lacking. They find the characteristics of myeloblasts as given by Naegeli, especially the number of the nucleoli, to be unreliable. Morawitz and Rehn consider the myeloblast the antecedent of the myelocyte. They found nothing to support the view that the myeloblast may represent a degenerated myelocyte.

## SURGERY.

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UNDER THE CHARGE OF

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**Some New Facts Concerning the Physiology of the Testicles and the Prostate.**—SERRALACH and PARES (*Annal. d. mal. d. org. gén.-urin.*, 1908, 1, 161), in studying the syndrome characterizing prostatic hypertrophy, were impressed particularly by the effect upon the function of the bladder. In the first period, that of congestion, the contractility of the bladder is equal to and sometimes greater than in the normal condition, although in the period of chronic retention the power of the bladder is much reduced. In nearly all cases the coefficient of contractility is increased after prostatectomy. This contractility has been observed at the end of the operation during irrigation of the bladder. A similar result has been observed after castration. A patient of Albarran with complete retention for six weeks, began to urinate spontaneously five hours after double castration. The retention in this case was rather the result of an inhibitory influence than of obstruction by the prostate. The authors hold that castration may produce atrophy of the normal prostate, but not of a pathological prostate. When atrophy does occur it takes three to six months to develop, so that it does not explain the rapid return of function already referred to. This rapidity can be explained best by a nervous effect. The effect produced by double castration is more marked than that by double vasectomy. The authors refer to two cases in which acute retention of urine had developed without apparent cause. In each case there was a history of sexual excess on the night before the development of the retention. They believe that an inhibitory effect is produced on the bladder by the testicles, and that this effect is removed by castration. From their experimental researches they are convinced that the prostate has an internal secretion which so acts upon spermatogenesis, and even upon the life of the testicle, that when one removes the prostate, atrophy of the testicles soon develops. This effect is indirectly like that of castration. The essential incontinence of children disappears spontaneously somewhere between one and fourteen years of age. The latter is the age at which the testicles usually begin to functionate, and thus to exert their inhibiting influence on the bladder. As the result of their experiments Serralach and Parés concluded that the testicles secreted a substance, X, which, when transferred into the circulation influences the contractility of the bladder. Its effect is to contract the membranous

urethra with more force than the neck of the bladder. It provokes relaxation of the bladder muscle. It increases the capacity of the bladder and delays the necessity for urination.

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**The Treatment of Spondylitis.**—WIENER (*Zentralbl. f. Chir.* 1908, xxxv, 252) says it is generally recognized that complete immobilization of the spine impairs seriously the respiration and digestion. The prevention of muscle spasm is sufficient. Wiener speaks favorably of Hessing's corset, and says that with it firm kyphosis may apparently be diminished by the addition of elastic traction. The cases in which the first four dorsal vertebræ are involved give the worst prognosis. Wiener reports a case of this kind in which a new method of treatment proved satisfactory. A woman, aged fifty-four years, had suffered for fifteen years from this condition. For a year she had experienced pain in the back which was transferred to the head, shoulders, and abdomen, and for six months she had been unable to get out of bed. The lower extremities could not be moved actively, and there was "foot drop," œdema of the feet and lower part of the legs. Clonic spasms of the legs occurred every few minutes, and these were accompanied by severe pain requiring heavy doses of morphine. These were due to the associated and renewed pachymeningitis. The pain was immediately relieved by weight extension to the head. At night a ten pound weight extension was applied in the usual way. During the greater part of the day the patient was placed in an easy chair and the weight extension was effected through a pulley in the ceiling. The patient was now able to perform active movements. To protect the head from being struck by the weight a special apparatus was suspended from a steel wire stretched tightly between two rooms. According to the needs of the patient the weight could be increased or decreased quickly by bags of shot weighing from one to five pounds. Wiener did not find it necessary to exceed ten pounds for the extension. The patient by means of this apparatus was moved from one part of the room to another. In a few days the clonic spasms were more rare and the first active movements occurred. After four weeks the patient could pass rapidly from one room to the other with the ten pound weight extension applied. In four months she could move freely, and in seven months she was discharged as completely healed.

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**The Origin of Median Cervical Fistulæ.**—WEGLOWSKI (*Zentralbl. f. Chir.*, 1908, xxxv, 289) calls attention to the fact that His, in 1880, showed that the origin of median cervical fistulæ was associated with the development of the median portion of the thyroid gland. It has not been explained why sometimes these fistulæ are lined with a single layer of epithelium, and at other times with several layers, and why its walls contain mucous glands, lymphoid follicles, etc. After a series of investigations upon 36 human embryos, 92 children, and 25 adult cadavers, Weglowski reached the following conclusions: In men, from an incomplete development of the median portion of the thyroid gland (in more than 30 per cent. of the bodies examined), there was found the remains of the primitive passage from the gland to the root of the tongue. This was either in the form of a separated small portion of the gland, a canal, or a cyst. These remains are usually not perceptible,

but may under favorable circumstances lead to the formation of goitres in unusual situations, or to fistulæ and cysts, the latter often becoming fistulæ later. The complicated microscopic structure of the fistulæ (single and several layered epithelial lining, lymphoid follicles, etc.) takes its origin from the mucous membrane of the root of the tongue, the isolated elements of which are drawn downward into the tissues by the developing median portion of the thyroid gland.

**A Communication on a Case of Operative Cure of Venous Thrombosis in the Region of the Superior Mesenteric Vein.**—HAAGN (*Deut. Zeit. f. Chir.*, 1908, xcii, 79) says that this is a very rare condition, and that the prognosis is very bad whether treated medically or surgically. The diagnosis in Haagn's case was made at the time of operation. The patient was a woman who had borne five children, the last being one and one-quarter years of age. After this birth she had suffered severe child-bed fever. The attending physician diagnosed pelvic cellulitis. The patient was ill for a half year. On the day of admission to the hospital, at 7 A.M., she was taken with sudden and severe pain in the abdomen, repeated vomiting, and no passage of flatus. A purgative produced two pulpy stools. Morphine did not control the pain. Examination revealed a specially painful area on the left side. During the manipulations the patient experienced a sudden movement, when the pain disappeared. The patient looked very ill, temperature 37.5°, and pulse 80. There was only slight distention, and to the left of the umbilicus could be palpated a sausage-shaped resistance, tender to the touch. Following a desire to defecate, she passed about a litre of pure fluid blood. Operation was delayed because of the improvement. The next day the symptoms were worse, and laparotomy was performed on the succeeding day. A median supra-umbilical incision permitted the escape of distended intestines, from among which there escaped a brownish red fluid. A sausage-shaped swelling which proved to be part of the jejunum, 20 to 30 cm. long, bluish red in color, without motion, and its walls several times their normal thickness was found on the left side. The corresponding portion of the mesentery showed numerous thrombi. The affected area formed a triangle, the base of which was at the intestine, the apex at the root of the mesentery. The peritoneal surface was lustreless and abundantly covered with fibrinous deposits. The ascending colon was drawn toward the attachment of the affected portion of the mesentery by a band, which was ligated and divided. The affected mesentery and bowel were resected and the divided ends united by a Murphy button. Drainage was employed. Eleven days later the presence of an intestinal fistula was recognized. Twenty days afterward the abdomen was re-opened on account of the symptoms of ileus. Several coils of intestine were found adherent to one another and one portion of bowel seemed to be acutely kinked, the proximal portion being distended. While correcting this flexion by separating adhesions, an opening was torn in the bowel wall. This was closed and the proximal portion of the bowel sutured into the abdominal wound for the performance of an enterostomy. Owing to the weakness of the patient the intestinal fistula was not closed. Seven months after the operation the patient was completely cured and could perform her usual work.



The sudden onset with vomiting and complete bowel obstruction made one think of strangulation ileus. The improvement in a few hours and the bowel movement, however, excluded it. Intussusception may develop in an elderly person, and, as in this condition, the bowels may move and blood be passed. This was Haagn's diagnosis. Kussmaul gives the symptoms of thrombosis of the mesenteric vessels as follows: Evidence of the source of the embolus; abundant hemorrhage from the bowel; subnormal temperature; peritoneal symptoms, as vomiting and abdominal pain. Haagn says that operation should not be done when the patient is in severe shock or has general peritonitis, and not as long as symptoms of paralytic ileus continue. Above all, one should determine as far as possible the probable extent of the gangrenous tissue. The best indication for immediate operation is the beginning of peritoneal symptoms. When anastomosis of the ends of the bowel after resection is possible, and one is sure that he has gone well into healthy bowel, this operation is to be preferred to a preternatural anus.

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**Syphilitic Dactylitis.**—CREITE (*Deut. Zeit. f. Chir.*, 1908, xcii, 70) believes that this affection begins in the soft tissues of the fingers, that it extends to the finger joints and bones, and finally results in considerable defects in the diseased bones. There develops slowly, with boring pain, a swelling in one finger joint, usually in the middle one. It is of a solid, almost bony consistency, is slightly bluish in color, and covered by tense, smooth skin. With variations in the degree of swelling there develops, in the course of weeks or months, an acute condition with more marked swelling, severe pain, and bluish discoloration of the skin. There is now seen a small vesicle about the size of a millet seed, with clear, watery contents, which, with the abatement of the acute symptoms dries up and in a few days disappears entirely. There is no perforation of the skin with ulceration and fistula formation. Rather does the swelling become smaller and the neighboring joints diseased and stiffened. The disease extends to the bones, with the development of defects in them and of shortening and deformities of the fingers. There was little or no effusion in the joint in Creite's case, but the surrounding soft tissues were actively involved in the inflammatory process. The joint did not suppurate, but the cartilages were involved and were quickly and completely absorbed. The original swelling of the bone was the result of a gummatous formation, which so affected the bloodvessels as to disturb the nourishment and lead to absorption of the bone without suppuration. As this rarifying osteitis proceeds, the inflammatory symptoms subside and disappear entirely, the color gradually becomes normal, and from the absorption of the bone the finger becomes considerably shortened.

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**A Case of Primary Renal Actinomycosis.**—KUNITH (*Deut. Zeit. f. Chir.*, 1908, xcii, 181) says that while actinomycosis of the kidney, secondary to some other focus, has been reported several times, up to the present only one case (von Israel) of the primary renal actinomycosis has been published. Kunith now reports a second case which occurred in a boy, aged four and three-quarters years, who, like v. Israel's patient, was operated on with successful result. The parents were healthy, but the grandparents and an uncle on the mother's side had died of phthisis. The

boy had had the ordinary diseases of childhood, and had always lived in Berlin, except for a stay of five or six weeks in the country when he was one and one-half years of age. In April, 1906, he fell from a swing, and as a consequence developed a swelling in the lumbar region. This swelling was twice incised by a physician, with the escape of pus. Two fistulæ resulted which would not heal. Four months before admission the patient suffered from temporary bladder trouble, and more recently the urine has been turbid, blood being passed on one occasion. For this he was brought to the hospital. He was slender, poorly nourished, and pale. His temperature and pulse were normal. The molar teeth of the lower jaw were carious, but the jaw was not swollen or carious. The heart and lungs were apparently normal and the abdomen soft. In the right kidney region was felt a firm resistance, and in the back on the same side below the tip of the twelfth rib was a granulating, suppurating fistula, and close by a second one. Below was a scar. The secretion from the fistulæ was very scanty, seropurulent, but without other peculiarities. A scab soon formed, and when a probe was introduced it passed only a short distance. A probable tubercular kidney was diagnosed and this was removed by what proved to be a rather difficult operation. In about four months the patient left the hospital completely healed, and eleven months after admission he had no further trouble and had improved very much in weight. From the fourth day after operation, for about five weeks, ray fungi were found in the urine. These consisted of an entanglement of threads, usually surrounded by a group of leukocytes. Clubs were found only twice, and these soon after the operation. Besides the actinomyces, the urinary sediment contained an abundance of leukocytes, blood for a short time after operation, and for a longer time hyaline and granular casts. Albumen disappeared completely from the urine only after four months.

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**The Permanent Results in Tuberculous Coxitis.**—PERRET (*Archiv f. klin. Chir.*, 1908, lxxxv, 561) says that tuberculous disease of the hip-joint has usually a very gradual, rarely a violent, acute origin. Direct and indirect traumatism, most frequently of mild grades, are the usual causes; infectious diseases and metastases more rarely. There is throughout, especially in young individuals, a considerable disposition to spontaneous cure; yet the frequency of relapses is a warning against a favorable prognosis. In young individuals the infection of the joint is secondary to a primary osteal focus; while in advanced age it is of synovial origin, except in those cases in which an old encapsulated, latent, osteal focus after years again becomes active. Tuberculous foci not in the wall of the acetabulum, but in its immediate vicinity, may invade the hip-joint; usually they do not. Primary foci in the head or neck of the femur sooner or later, as a rule, break into the joint. A coxitis of pelvic origin may have in the early stages, apparently, as favorable a prognosis as that of femoral origin. In the later stages, however, it develops an extensive caries of the acetabulum, in which resection of the joint may be without good results. The best functional results were obtained by conservative operations, especially by early arthrotomy with sequestrotomy or erosion of the tuberculous focus. Conservative treatment gave good results, although it was not always sufficient, and

in half of the cases it was necessary to substitute conservative operations, especially resection. In mild, favorable cases with or without enclosed suppuration, in which the seat of the focus cannot be determined with certainty either by clinical examination or by the *x*-rays, the treatment should be conservative until the osteal focus is evidently not undergoing spontaneous healing, but is recognizably extending. In neglected severe cases, with open sinuses and with other threatening complications, arthrotomy for the exploration of the joint should be carried out. When the joint is so destroyed that there is no hope of spontaneous healing, all the diseased tissue should be thoroughly removed and the healthy tissue saved, "atypical resection." Perret hopes that typical resection, that is, decapitation or still more, subtrochanteric excision, will gradually disappear. When by an exact clinical investigation the tuberculous focus can be localized, and this can be confirmed by the *x*-rays, our present day aseptic arthrotomy with sequestrotomy, or erosion of the diseased part, will give the best results from the standpoints of time, radical healing, and functional results.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**Oil Injections in Constipation.**—VIDAL (*Journal de médecine de Paris* (1908, xx, 2) advises the use of irrigations of sterile alcohol-free oil in constipation. A fountain syringe is employed to which a soft rubber catheter, which is passed about 3 inches into the rectum, is fitted. The oil is introduced about two hours after the evening meal, the patient lying on his back or left side. The quantity given is from about 2 to 7 ounces, and its temperature should be about 95° F. After the tube is inserted the reservoir of the syringe is elevated to about 3 feet above the patient and the oil is allowed to flow slowly into the rectum. Should there be difficulty in inserting the tube, the rectum should be cleared by means of an irrigation of saline solution. The oil should be retained all night, and in the morning, on rising, an irrigation of about a pint of saline solution at 100.5° F. is taken. This should be retained for a few minutes. The oil injections are given daily at first, but after a week the intervals may be lengthened until one every five days becomes sufficient. The treatment may, at first, cause colicky pains, but these soon cease.

**Flexner's Serum in Epidemic Meningitis.**—DUNN (*Boston Med. and Surg. Jour.*, 1908, clviii, 370) has used Flexner's antiserum in 15 instances of epidemic cerebrospinal meningitis, in all but one of which the diagnosis was confirmed by finding *Diplococcus intracellularis* in the cerebrospinal fluid. Of these instances, 8 have resulted in complete recovery, 2 have died, and 5 are still pending. The 8 patients who have recovered are all perfectly well, having been left with no sequels of any kind. The 2 fatalities were both in chronic infections, in which the disease had run considerable time before coming under observation. Of the 5 instances still pending, 4 will undoubtedly recover; the other is a chronic infection, and in it the outcome is dubious. Each of the 8 patients who received the serum in the first week of the disease has completely recovered, and of the pending instances, 2, in which the antiserum was given early, are convalescent. The most important point suggested by the results attained is the advantage to be gained by giving the serum early in the disease, and it seems impossible to overestimate the value of early diagnosis and treatment. It would seem that the results obtained with this serum in the patients reported are sufficiently good to afford strong basis of hope that this treatment will prove of a value commensurate with that of the antitoxin treatment of diphtheria, and, although the treatment requires further testing, the author believes that the serum should be used in every instance of this disease and as early as possible. The serum is injected into the spinal canal by means of a lumbar puncture. As much fluid as will run freely is allowed to escape, then the syringe is filled with the antiserum and is connected with the needle through which the fluid has escaped, and the serum is injected. Flexner suggests  $7\frac{1}{2}$  drams as the maximum dose, to be repeated for three or four days, and that at least as much cerebrospinal fluid as this should be first withdrawn in order to avoid risk of unduly increasing the cerebral pressure.

**The Toxicity of Therapeutic Sera.**—BESREDKA (*Revue médico-sociale*, 1908, ii, 10) holds that the toxicity of therapeutic sera should be tested by making injections of the sera into the brains of guinea-pigs. Such tests show that different sera possess different powers of toxicity, the fatal dosage varying from  $\frac{1}{2}$  c.c. to  $1\frac{1}{2}$  c.c. Sera from horses living under similar conditions possess practically the same toxic powers, variations being rare and of little importance. Variations in the toxicity of sera seem to be due, first, to their origin, second, to their age. A serum hypertoxic when fresh loses, little by little, its toxic qualities; this loss, rapid at first, gradually becomes slower, and ceases by the tenth day. All therapeutic sera should, however, be considered to possess toxic qualities for two months after they have been drawn. In general, every serum which causes grave anaphylactic phenomena in doses of  $\frac{1}{16}$  to  $\frac{1}{2}$  c.c. or less should be considered as toxic. The technique of the intracerebral injection is simple, rapid, and not expensive.

**Bacterial Vaccines in Septicemic Conditions.**—BRISTOW (*New York State Jour. Med.*, 1908, viii, 120) reports the results in four patients in whom vaccine treatment was attended with excellent effects. Two of the patients suffered from a streptococcic septicemia, a third was afflicted with furunculosis, and the fourth possessed a gonorrhoeal arthritis.

Each of these was treated with injections of an appropriate vaccine. No conclusions are drawn, since the number of patients is so small, but the fact that the vaccine treatment succeeded when other measures had signally failed is most suggestive.

**Colloid Metals in Therapeutics.**—CAPEZZUOLI (*Zentralbl. f. die ges. Therapie*, 1908, xxvi, 113), in a paper under this title, cites 24 instances of appendicitis, reported by Moosbrugger, which were treated by colloidal silver. Of the 24 patients, only 2 died, and these exhibited the symptoms of severe peritonitis before treatment was begun. The colloidal silver was given internally in doses of a tablespoonful every half to one hour of a 0.5 to 1.5 per cent. solution; twice a day 30 grains of unguentum Credé was rubbed into the skin, and twice daily enemas of  $7\frac{1}{2}$  grains of colloidal silver in 3 ounces of water were given. Children received one-fourth of the above doses. In most of the patients improvement was evident in two days, and upon the third the fever and local symptoms abated. In the severer instances improvement was evident in from four to eight days. The author compares the action of colloidal silver in appendicitis to that of antitoxin in diphtheria.

**Intravenous Injections of Colloidal Silver.**—FRANCKE (*Medizinische Klinik*, 1908, iv, 12) states that in grave infectious processes, such as sepsis, puerperal and otherwise, colloidal silver should be employed in 4 to 5 per cent. solution as an intravenous injection, 30 grains being injected daily or every other day, according to the type of the affection and the effect of the remedy. In one instance of severe gonorrhœal sepsis, with chills persisting for weeks, one such injection brought about a rapid and permanent fall of temperature. Injections of colloidal silver are usually followed by a chill succeeded by a rise of temperature even as high as  $105.8^{\circ}\text{F.}$ , but this phenomenon has no untoward sequels. The employment of this agent by intravenous injection is superior to its exhibition by enema or inunction, and the former is the preferable mode of administration.

**Quinine Hydrobromide in Exophthalmic Goitre.**—JACKSON and MEAD (*Boston Med. and Surg. Jour.*, 1908, clviii, 346) recapitulate their results with this drug as follows: 42 patients cured (no signs or symptoms for two years), or 76 per cent.; 7 patients benefited, or 13 per cent.; 6 failures, or 11 per cent. It is not claimed that the cures are permanent, yet the patients are free from symptoms and signs and are able to perform their work. In addition to the use of the quinine, general treatment, such as rest, diet, care of the stomach, intestines, and skin, was instituted. Quinine hydrobromide is a combination of quinine and hydrobromic acid in which all the bonds are satisfied and we have a neutral salt with a formula,  $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2\cdot\text{Br} + \text{H}_2\text{O}$ . In order to get the best results the salt must be the neutral, not the acid salt. The dosage is 5 grains in capsules three times a day; this is as much as is ordinarily well borne, but some patients may be able to take 4 capsules daily without tinnitus; others cannot take more than 2 capsules a day. The patient should be told that he should expect little or no benefit short of a month, and that the treatment must be continued for at least two years. Usually, after a week or two the pulse rate will be slowed,

the thyroid diminished, and the sweating or tremor lessened. The treatment should be continued until all the symptoms have disappeared, which may be in four months or not for three years. No bad effects have been noticed to follow the treatment, and the only unpleasant action of the drug is occasional tinnitus, especially if large doses be given. Relapses are not rare, but if taken in hand quickly usually yield readily. The author does not attempt to explain how the quinine acts, but is convinced that it has a distinct curative effect.

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**The Physiological Action of Iodothyrim.**—VON FURTH and SCHWARTZ (*Klin.-therap. Woch.*, 1908, xv, 209) have examined animals in which a condition of hyperthyroidism had been induced by means of the administration of thyroid preparations (iodothyrim) and in which Loewi's phenomenon (pupillary dilatation following instillation of adrenalin into the eye) had been induced. The results of the experimentation appeared to show that iodothyrim is not the only principle contained in the thyroid gland. After intravenous injection of iodothyrim in cats the blood pressure falls and the pulse rate becomes less, due to stimulation of the vagus centre in the medulla; even temporary cessation of the heart action may be induced. Artificial iodothyrim has the same action; iodothyrim is a complex iodine derivative which is contained in an albumin molecule.

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**Drugs in Diabetes.**—ELLIOTT (*Illinois Med. Jour.*, 1908, xiii, 312) considers that it is inviting failure to give a drug cure to a diabetic, and by beginning the treatment with drugs, the patient, ever prone to believe in the occult power of medicine, comes by degrees to rely upon this part of his treatment rather than upon the infinitely more valuable dietary rules; he naturally tends to follow the path of least resistance, and prefers his capsules or drops to the more arduous self-denying system of diet. Of the drugs usually given, opium is the first on the list, but its long-continued and indiscriminate administration is unjustifiable. It exerts no specific action, and its effects on a given patient cannot be foretold. It may predispose to coma, and there is the danger of habit formation. Antipyrine, acetanilide, aspirin, and the salicylates may depress the patient, cause cardiac irritability, and have been known to induce albuminuria. In gouty patients the salicylates may be of benefit. Jambul has never proved of use in the author's hands. Arsenic has no specific effect, but small doses act well on general nutrition, and may do good. The alkalies are of distinct value. They may be given in the form of mineral waters or as one of the medicinal salts, carbonates, bicarbonates, citrates, or tartrates, the sodium salts being preferable. The dose will depend on the stage of the disease and the degree of the acid toxemia. In severe types of the latter alkalies act as a prophylactic of coma, and must be given in large doses. Patients whose urine contains acetone should receive at least a half-ounce of sodium bicarbonate daily, and if coma is impending two to four times this amount should be given. In constipation sodium citrate may be added to the bicarbonate with advantage, and the additional employment of calcium carbonate to replace the calcium waste characteristic of diabetes has been suggested.

## PEDIATRICS.

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UNDER THE CHARGE OF

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**Needle in the Left Bronchus.**—H. VON SCHROETTER (*Deut. med. Woch.*, 1908, xxxiv, 641) reports the case of a girl, aged twelve years, who had swallowed a shawl pin, 74 mm. (3 inches), long, the glass head of the pin had a diameter of 9 mm. The pin entered the left bronchus head first, the latter being in one of the divisions going to the lower lobe at the time the Röntgen picture was taken. Twenty-one days after the accident Schroetter removed the pin by bronchoscopy using a tube 21 cm. long and 8.5 mm. in diameter. Local anesthesia was employed and the needle grasped at the third attempt and pulled out without injury to the bronchial structures. No disturbances developed, the patient remaining perfectly well.

**The Treatment of Diphtheria with Pyocyanase and the Persistence of the Diphtheria Bacillus.**—P. L. SCHLIPPE (*Deut. med. Woch.*, 1908, xxxi, 588) has employed pyocyanase in the treatment of 54 cases of diphtheria of varying degree. Several cubic centimeters of pyocyanase were dusted energetically upon the diseased portion of mucous membrane four times daily, the treatment being divided into two parts, with an interval of five to ten minutes between applications. According to various observers the favorable action of pyocyanase depends on its bactericidal action, in its power of impeding the development of bacteria, of neutralizing their toxins, dissolving the diphtheritic membrane, destroying the pathogenic organisms upon which the mixed infection depends, and, finally, upon favoring the restitution of the mucous membrane. In a number of cases no antitoxin was employed; in some of these, and particularly the lighter cases, the membrane disappeared very quickly and the symptoms diminished with it; in one instance only one side was thus treated and the membrane persisted on the untreated side. A piece of membrane treated with pyocyanase in a test-tube at blood heat dissolved in a similar manner. In other cases, however, the pyocyanase did not seem to suffice and antitoxin had to be injected, as the process spread further, or the toxic symptoms increased to an alarming degree. All these patients improved at once as soon as the serum was injected; 24 of the patients were treated with serum and pyocyanase simultaneously. In 9 the specific action of the powder was noted, in 9 others it was not, and 6 died in spite of both measures. When the trachea was affected the pyocyanase blown into the trachea through a cannula did not influence the course of the process. Concerning the persistence of the organism 46 patients were studied; in 4 no bacilli could be found after the first week, in 3 after the second week, in 5 after the third, and in 5 after the fourth week; in all others the bacilli persisted more than a month and in some considerably longer,

even if pyocyanase was blown into the nose and pharynx. Chronic diphtheria developed in a number of them. This persistence is probably due to the fact that the pyocyanase cannot enter all the crypts of the nasopharynx in which the bacilli vegetate. Schlippe comes to the following conclusions: Pyocyanase must never be used in the treatment of diphtheria without simultaneous injection of serum. In some cases the pyocyanase seems to quicken the solution of the diphtheritic membrane, to remove the *foetor ex ore* at once, and to produce immediate subjective improvement. It deserves to be employed further, therefore, in cases of intense membrane formation and when the membrane persists abnormally long. In very grave cases of septic diphtheria the pyocyanase does not seem to have any influence. Pyocyanase does not prevent the persistence of the diphtheria bacilli, nor does it kill the bacillus in instances of marked persistence and chronic diphtheria.

**Bradycardia in Appendicitis of Children.**—J. VON BOKAY (*Deut. med. Woch.*, 1908, xxxiv, 649) reports briefly the histories of 10 cases of appendicitis in children, all of whom presented marked bradycardia at some time during the disease. He deduces the following conclusions from the study of his cases: (1) During the period of absorption of peri-appendicular inflammatory exudate bradycardia may be said to be almost the rule and may exist over several days, even more than two weeks. (2) It may also appear after incision of an appendicular abscess and may persist eventually for days. (3) It may also follow resection of an appendix when the operation is performed later during the quiescent stage and may then also persist for some time. (4) The number of pulse beats may fall in children of between seven and sixteen years to 52; in most of Bokay's cases the pulse varied during the period of bradycardia between 52 and 80. (5) The pulse and temperature curves during the period of bradycardia do not run parallel to each other; hyperpyrexia was never observed when the pulse had fallen to the minimum. (6) This bradycardia cannot be considered as an unfavorable symptom from a prognostic standpoint; in cases of peri-appendicular exudate it is even to be considered as a sign of a beginning absorptive process.

**The Late Results of Tracheotomy.**—W. WOLF (*Deut. med. Woch.*, 1908, xxxiv, 725) reports that at Trendelenburg's clinic tracheotomy was performed in 404 children between the years 1895 and 1906; 140 (31.3 per cent.) of these died, but in no instance could the fatal termination be laid to the operative interference. He compares this mortality with that of 1539 cases, in which intubation was performed and in which the fatality percentage amounted to 31.7 per cent., thus showing that the mortality from the two operations is the same. Of the remaining 264 children personal examination or letter reports were had of 173. Subsequent to the diphtheria there were 4 deaths from other causes, 145 presented no disturbances whatever, and only 24 (14.2 per cent.) had disturbances of varying degrees. In 7 the disturbance was of a more serious nature, it being tuberculosis, however, only in 4 cases, and 3 of these had an inherited disposition to the disease. Even if the disturbance in all of these 24 individuals could be traced directly to



the tracheotomy (which seems highly improbable), this figure shows conclusively that tracheotomy is not followed in many cases by late and serious indisposition. In no instance did a cicatricial stenosis develop, which, according to the opponents of tracheotomy, is a very common sequence. In the paper on intubation above mentioned, Wolf records 16 cases of cicatricial stenosis due to pressure decubitus. The splendid showing at Trendelenburg's clinic is probably due to the fact that he always performs inferior tracheotomy, which predisposes less to stenosis than superior tracheotomy. The statement made by the defenders of intubation that tracheotomy should never be performed because of the possibility of the cicatricial stenosis developing, or of a possible injury to the deeper-lying air passages (due to loss of heat which inspired air ordinarily gets in the nasopharynx) is negated by Wolf's statistics.

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**The Pepsin Secretion of the Healthy and the Sick Nursling.**—The method employed by J. ROSENSTEIN (*Berl. klin. Woch.*, 1908, xlv, 542) follows the principle that castor oil made turbid by the addition of hydrochloric acid is cleared up only by pepsin: filtered gastric juice was diluted in varying degrees and experiments performed to show at which dilution a certain quantity of turbid castor oil solution was still clarified. He found that the amount of pepsin in the healthy, artificially nourished infant increases with age until after the end of the third month of life; from then on it remains constant. Healthy, breast-fed infants seem to produce less pepsin, than healthy, artificially fed children of the same age. Older nurslings of less weight than normal produce the amount of pepsin which corresponds to their age. Disturbances in nutrition do not influence pepsin secretion markedly; if decomposition be present a lessening in the amount of pepsin is noted. The lack of ferment (particularly the lack of pepsin) is of slight symptomatic importance and is certainly not an etiological factor in the production of digestive disturbances of nurslings.

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**The Value of Pirquet's and Wolf-Calmette's Reaction in Children.**—R. BING (*Berl. klin. Woch.*, 1908, xlv, 546) has employed Pirquet's test in 241 patients, 19 of whom were certainly tuberculous, 36 suspicious, and 186 not tuberculous. A positive reaction was obtained in 14 of the first (73.7 per cent.), in 25 (69 per cent.) of the second and 34 (18.2 per cent.) of the third. Wolf-Calmette's reaction was tested in 100 cases, which were distributed over the three classes as respectively 6, 15, and 79 patients; positive reaction was obtained in respectively 3, 6, and 1 patients. He therefore considers both methods valuable and especially are the positive results in early childhood to be valued as regards the diagnosis of tuberculosis; a negative result does not necessarily mean absence of tuberculosis. If both methods show a negative result in clinically doubtful cases, the probability of tuberculosis is very likely. Pirquet's test is valuable also in cases of latent tuberculosis. Pirquet's method is without danger; the conjunctival reaction, however, is sometimes followed by violent inflammation and other unpleasant sequels, which have made Bing cautious in its use, and in the case of scrofulous children have forced him to forego it absolutely.

## OBSTETRICS.

UNDER THE CHARGE OF

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**The Healing of Pubiotomy Wounds.**—OBERNDORFER (*Zentralbl. f. Gynäk.*, Nr. 7, 1908) contributes an interesting paper with macroscopic and microscopic illustrations upon this topic. He reports the case of a multipara who was delivered of a child weighing nine pounds, by pubiotomy upon the right side of the pelvis. The patient recovered from the operation, but died fourteen months afterward from some intercurrent disease. The pelvis was secured for examination. On studying the specimen by the *x*-rays, it was found that the wound inflicted by the saw had healed without the slightest appearance of the formation of bone. Microscopic examination of the specimen showed that there was no deposit of true bony tissue. This seemed to have been prevented practically by fibers of elastic and connective tissue which extended throughout the substance between the ends of the bone. This seems an unusual result, as in the case of fractures in young individuals bony tissue is rapidly deposited, although the separation of the fragments may have been greater than after the operation of pubiotomy. The most reasonable explanation of the difference lies in the fact that the pubiotomy wound has sharply defined edges, while in the case of fracture splinters of bony tissue, small portions are irregularly projecting, and thus form centres of ossification. There seems to be no essential change in the condition of the parts as late as a year after the operation.

**Chorio-epithelioma Developing after a Full-term Pregnancy.**—WENZEL (*Zentralbl. f. Gynäk.*, Nr. 7, 1908) reports the case of a woman who had borne a healthy, vigorous child at the normal period of gestation. Six weeks after labor she had irregular hemorrhage, for which a curetting was done, a large quantity of necrotic tissue, apparently connective, being removed by the curette. The irregular hemorrhage continued, and the curette removed necrotic tissue from the interior of the uterus. On examination, this proved to be chorio-epithelioma. In order to be sure of the diagnosis before sacrificing the uterus, a second curetting was done, with the same result. The uterus was then removed. Eight months afterward the patient was well. The interesting point in the case consisted in the development of the malignant growth after a perfectly normal pregnancy going to full term. The diagnosis was based entirely upon the microscopic examination of the tissue removed, as the patient presented no symptom of the condition.

**Pregnancy Complicated by a Necrotic Myoma.**—SCHENK (*Zentralbl. f. Gynäk.*, Nr. 7, 1908) reports the case of a patient pregnant for the first time, between the seventh and eighth month, whose pregnancy was complicated by a myomatous tumor. On examination, the abdo-

men was much distended; the tumor was composed of two portions, the lower of which extended four fingers' breadth above the pubes and seemed to contain the foetus. The upper portion of the tumor was softer in consistence, and separated from the lower by a groove in which the finger could be laid. The condition of the patient improved very considerably, with rest in bed; the pulse and temperature became nearly normal, and operation was finally performed. The uterus was amputated at the vaginal junction and the right tube and ovary were left. The patient made a good recovery. On examination, the upper portion of the tumor was found to be a necrotic myoma which comprised four-fifths of the entire mass. In the lower portion was a foetus about five months in development. The tumor had grown very rapidly during pregnancy, had prevented the development of the child, and rendered spontaneous labor impossible.

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**Retention of the Foetal Membranes and its Treatment.**—LOUROS (*Zent. f. Gynäk.*, Nr. 7, 1908) reports 7 cases of retention of the foetal membranes, and concludes that several interesting questions arise in connection with this subject. He believes that just as much pains should be taken to secure the entire removal of the membranes as of the placenta. He also believes that the same care should be exercised in examination, and that should a diagnosis of retained membranes be made, the hand or sufficient fingers should be inserted, under antiseptic precautions, to remove them completely. If a very small portion of the membranes is left behind this may be allowed to remain, as it will be finally brought away in the lochial discharge. If during the pregnant period hemorrhage, fever, and foul lochia develop, the uterus should be explored to discover and remove the retained membranes. In cases in which the placenta has been expelled, but the membranes remain held within the uterus, the operator must use great caution lest the membranes be torn away from the placenta and a portion retained.

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**Recent Advances in Obstetrics.**—CRAGIN (*Amer. Jour. of Obstet.*, March, 1908) contributes an article upon this subject, calling attention to recent advances in obstetrics, with a better knowledge of obstetric pathology, a better knowledge of the mechanical problem of delivery, and a better procedure. He draws attention to the pathology of toxemia, which he divides into the nephritic and hepatic types. He also recognizes pernicious nausea as a toxemic process. His paper contains illustrations of microscopic slides from the kidney and liver, illustrating the points studied. He believes that a second important advance in pathological knowledge is our increased knowledge of chorio-epithelioma malignum, especially in the matter of its diagnosis.

In the pathology of puerperal infection, we have come to appreciate the ease with which infection from without can be conveyed to the vagina or uterus, and also the danger of manipulation of the uterus in sepsis, which may change a local into a general infection.

Under the heading, "A Better Knowledge of the Mechanical Problem of Delivery," Cragin calls attention to the fact that we must not rely upon external pelvimetry, but must study the size of the foetal head and its adaptation to the pelvic brim and cavity. Improvement in the

management of posterior rotation of the occiput through an early diagnosis and methods adapted to secure anterior rotation, are also of importance. Careful watching of the foetal heart during labor, the cephalic application of the forceps, and in some cases rotation by forceps, are all indicated.

The importance of the nitrogenous partition of the urine is emphasized, and the fact that laboratory findings alone do not give ground for a choice of treatment unless taken in connection with the clinical study of the case. In pernicious nausea, irrigation of the colon, rectal feeding for a short time only, and early emptying of the uterus are the methods of treatment which have given the best results.

When menorrhagia or metrorrhagia persists after labor, chorio-epithelioma should be suspected, and early operation performed if a diagnosis can be made.

In the treatment of septic infection, uterine manipulation should be avoided when once the uterus has been relieved of that infected material which is ready to be discharged. The induction of labor in patients who have had difficulty in previous parturition, should be chosen when it is evident that the head is not proportionate to the pelvic canal. In cases in which the pelvis is not unusually large the prolongation of pregnancy should not be allowed to reach an extreme limit. Craniotomy has been made an infrequent operation by the improvement in Cesarean section and methods of inducing labor. Pubiotomy in hospital practice will save some children who might otherwise be lost. When mechanical dilatation is impossible, vaginal Cesarean section may be chosen.

Cragin believes that in proper surroundings, with good light and proper assistance, a well-trained man may repair with advantage laceration of the cervix immediately after labor. Unless these conditions are present, he believes that the cervix should be closed by suture in cases of hemorrhage only.

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**Extra-uterine Pregnancy.**—IWASSE (*Archiv f. Gynäk.*, 1908, lxxxiv, Heft 2,) reports 38 cases of tubal gestation in the clinic at Tokio. His conclusions from the study of these cases are as follows: Comparing these cases with those reported in European clinics, he finds no especial difference in the origin or manifestation of ectopic gestation among Japanese and Europeans. This condition is most frequent between the twenty-fifth and thirtieth years of life; 86.8 per cent. of the patients had not previously borne children. Extra-uterine pregnancy was frequently preceded by a period of relative sterility. Its occurrence was also frequent after abortion. It seems probable that operations for correcting the position of the uterus, such as ventrofixation or intraperitoneal shortening of the round ligaments, may tend to produce ectopic gestation. Tubal abortion is most common during the first and second months of ectopic gestation, and rupture during the third and fourth months. Abortion is more frequent than rupture. When extra-uterine pregnancy goes to viability the foetus is more apt to develop malformations and anomalous positions and presentations. Hemorrhage from the uterus and pain in the abdomen are important symptoms, usually appearing together, or separated by a short interval—not more than a week. Migration of the impregnated ovum in extra-uterine pregnancy is rarely observed.

## GYNECOLOGY.

UNDER THE CHARGE OF

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**Kraurosis Vulvæ.**—A. W. RUSSELL (*Glasgow Med. Jour.*, December, 1907) attributes the pruritis accompanying kraurosis vulvæ to discharges from the tumor or to diabetic urine. In the treatment he recommends physiological rest of the parts, thorough cleanliness, the care of uterine, intestinal, or vaginal disorders, local application to the vulva, and excision of the parts. He advises excision. The radical treatment should not be carried out too late.

**Primary Carcinoma of the Fallopian Tube.**—E. KEHRER (*Monatsschrift f. Geburtsh. u. Gynäkol.*, 1908, xxvii, 327) reports a case of carcinoma of the right tube, and reviews the 79 cases of tubal carcinoma previously reported. According to another, tubal carcinoma cannot be differentiated from pyosalpinx by location, form, size, consistency, or adhesions. For this reason a probable diagnosis of tubal carcinoma has been made only twice, and a certain diagnosis only once. A rapidly growing tumor in the cul-de-sac and a hemorrhagic exudate withdrawn through a puncture in the vaginal vault are significant. Tubal carcinoma is considered more malignant than carcinoma of the cervix or fundus, on account of the thin walls of the tube and its rich lymphatic supply. A radical operation performed as early as possible is therefore indicated. Kehrer does not believe that tubal carcinoma is necessarily preceded by inflammatory changes, as held by Säger-Barth, and he would differentiate between papillary carcinoma of the tube and alveolar carcinoma merely as early and late stages of the same process.

**Results of the Radical Abdominal Operation for Carcinoma of the Uterus.**—E. WERTHEIM (*Zentrbl. f. Gynäkol.*, 1908, xxxii, 175) gives the results of his first 120 operations for carcinoma of the uterus by the method which bears his name. These operations were performed over five years ago. Of a total primary mortality of 27, 14 deaths occurred in the first 30 cases and 13 in the remaining 90. Excluding from the 93 cases in which recovery followed the operation 3 cases of carcinoma of the fundus, 1 case of carcinoma of the vulva, and 2 cases in which death was not due to cancer, Wertheim has 87 cases which have now been under observation for five years since operation. In 51 of these cases, or 58.6 per cent., there has been no return of the disease. Of 4 cases in which carcinomatous glands were removed, 3 have shown no return. Wertheim has now performed over 400 operations of this character, and without lessening in any way the thoroughness of the operation, has greatly reduced the primary mortality, so that in the last 158 cases there were only 12 deaths, or a mortality of 7.5 per cent. That the operation as performed is still radical is indicated by the fact that in

the last 158 cases necrosis of the ureter and fistula formation occurred in 10 cases. In 7 of these the fistula healed spontaneously. The improvement in technique, to which is attributed the diminished mortality, relates primarily to a better control of hemorrhage.

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**Phlebitis following Abdominal Operations.**—O. G. PFAFF (*Amer. Jour. Obst.*, 1907, lvi, 630) states that this distressing complication occurs in 2 per cent. of all abdominal operations, and draws the following conclusions: (1) Many of these cases are simply extensive aseptic blood clots, without any true inflammation. (2) An abnormal plasticity of the blood must be present in order that thrombosis may be the result of surgical traumatism. (3) The clot generally receives a mild form of infection introduced into the wound at the time of the operation, and in turn an invasion of the vein wall results. (4) As stagnation is such an important element in the etiology, getting our patients up earlier will undoubtedly reduce the liability to thrombosis. (5) As an abnormally high degree of plasticity of the blood is essential in developing the disorder, the blood ought to be tested by some recognized standard in every case, and, if found in a dangerous state, operation should be postponed until medication shall have brought it back to a normal condition.

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**Neurasthenia in its Relation to Pelvic Symptoms in Women.**—E. A. WEISS (*Amer. Jour. Obst.*, 1908, lvii, 230) believes that neurasthenic pelvic symptoms in women frequently exist without pathological changes in the pelvis; that a careful differentiation between neurasthenia and real morbid anatomy must be made before deciding on the treatment, and that this form of neurasthenia is not only unimproved but frequently aggravated by surgical treatment.

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**Protrusion of the Uterus in Nulliparous Women.**—GEORGE ERETY SHOEMAKER (*Jour. Amer. Med. Assoc.*, 1907, xlix, 2151) reports two cases of protrusion of the uterus in nulliparous women and endorses the statements of other observers that heavy lifting, pelvic deformity, and the steady downward pressure of various tumors, such as ovarian dermoid cysts, are the usual causative agents. Shoemaker inveighs against radical exsections for relief of the condition mentioned.

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**Fibroid Operations during Pregnancy.**—J. H. CARSTENS (*Amer. Jour. Obst.*, 1907, lvi, 736) reports 7 cases of operation for fibroid during pregnancy, with 1 death. One, a myomectomy case, had a very long pedicle and fibroid complicating a three months' pregnancy, and went to full term; another had fibroids complicating a five months' pregnancy; myomectomy was done, and two months later the uterus was spontaneously emptied. In a third case no result is known. In 2 others prompt abortion followed, while in the remaining case hysterectomy was done.

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**The Frequency and Significance of Endometritis.**—B. M. ANSPACH (*Jour. Amer. Med. Assoc.*, 1908, l, 842) states that the classification of endometritis by different writers is lamentably at variance. In six text-books taken at random twenty-seven different varieties of endometritis were described, and not a single one of them was mentioned in

each book. Anspach says the presence of a discharge is in a large number of instances regarded as *prima facie* evidence of endometritis and that such practice exaggerates the importance of the endometrium in the eyes of the general practitioner. Anspach believes that but a small portion of the cases curetted for endometritis have changes in the mucosa demonstrable with the microscope. He examined the endometrial scrapings from 174 cases of dilatation, and curettage and in 80 of them the report was "normal." In 81 cases of repair or amputation of a lacerated cervix the endometrium was normal in 15; in 78 hysteromyometomies the endometrium was normal in 11; in 60 cases of pelvic inflammatory disease the endometrium was normal in 12, and in 53 of retroposition of the uterus it was normal in 24. Anspach insists that the endometrium is not abnormal in fully half the cases diagnosed as endometritis and offers a warning against encouraging hope of stopping leukorrhœa by curettage.

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**Tubal Twin Pregnancy.**—CHARLES G. CHILD, JR. (*Jour. Amer. Med. Assoc.*, 1907, xlix, 2134) reports a case of tubal twin pregnancy, which he says is the sixth to be reported, the other 5 being those of Schauta, Sanitor, Cameron, McConn and Henricius, and Koester. In addition, Child says his is the first in which the fetuses were of equal size, and the second (McConn's being the first) in which both were in one amniotic sac.

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**Unrecognized Gonorrhœa in the Female.**—S. W. BANDLER (*Jour. Amer. Med. Assoc.*, 1908, l, 335) believes that very commonly the gonorrhœal nature of vaginal discharges and vague pelvic pains, sterility, absolute or relative, profuse menstrual flow, and chronic, mild urethritis is overlooked. Bandler believes that chronic prostatic gonorrhœa often causes chronic gonorrhœa in the female, giving rise to an entirely different clinical picture from that of acute gonorrhœa.

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**Final Results of Conservative Surgery of the Tubes and Ovaries.**—ABRAM BROTHERS (*Jour. Amer. Med. Assoc.*, 1908, l, 595) reports having practised so-called conservative surgery of the uterine appendages in 158 cases. In but 85 of these subsequent reports are available, though Brothers states he earnestly requested patients to report to him. He frankly admits that in the presence of pus in the Fallopian tubes excision of the tube is the preferable procedure, although ovaries apparently normal in appearance that are in juxtaposition to such tubes or pelvic pus collections can safely be left undisturbed or may be subjected to partial excision. Brothers says, "These ovaries, if not the seat of abscess at the time of operation, seldom, in my experience, give rise to trouble later." Many gynecological surgeons will heartily commend his practice of removing by the abdominal route the pregnant Fallopian tube, although some so-called conservatives will advocate saving such structures. In considering the treatment of pus tubes Brothers states: "My practice is in favor of total and complete ablation of pus tubes down to the horn of the uterus. Experience with secondary operations for infected stumps has driven me to this position." Brothers estimates 23.5 per cent. morbidity after conservative operations on the tubes and ovaries in his practice. This estimate is based upon observation of half

his patients for periods varying from one month to twelve years. It is more than probable that the proportion of failures was much higher among the non-reporting patients than among those subsequently under observation. This statement is based largely upon the much larger proportionate number of women that apply for treatment after operations of a conservative nature done by other surgeons as compared to operations of a radical nature. The experience of many gynecologists in operations following "would-be" conservative operations by themselves and by others has driven them to abandon the "conservative" plan.

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## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

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UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,  
OF PHILADELPHIA.

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**A New Method of Entering the Maxillary Sinus through the Nose.**—VAIL (*Laryngoscope*, January, 1908) penetrates the wall of the antrum with a special perforating bistoury, with which he then enlarges the cut, forward and backward, to permit the introduction of a special grooved saw, with which he saws out a large piece, making a large oval opening in the wall. In this operation sacrifice of the anterior portion of the inferior turbinate is avoided.

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**New Operation on Accessory Sinuses of the Nose.**—WILLIAMS (*Bristol Med.-Chir. Jour.*, March, 1908) contributes an illustrated lecture on suppurative diseases of the nose and ear, with special reference to some newer methods of treatment. Williams' method, for which we have not space to detail, is an osteoplastic procedure which gives very free access to the ethmoid cells, sphenoidal sinus, and frontal sinus, and yet avoids the destruction of the nasal bone; and above all does not leave a depressed pit below the bridge, because no bridge has been made.

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**Trichinosis of the Upper Respiratory Passages.**—MACKENTY (*Amer. Med.*, February, 1908) reports 4 cases, in 2 of which throat symptoms predominated in the form of cedema of the larynx. Three lived in the same house and the other in the same block. All of them gave a history of eating ham bought from a store in the vicinity.

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**Serum Therapy in Epistaxis.**—SCHIFFERS (*Arch. Internat. de Laryng., d'Otol., et de Rhin.*, January and February, 1908) discusses this subject and reports 2 cases of his own, one in a hemophilic and one in a subject of essential purpura, in which the dyscrasia was successfully combated by hypodermic injections of fresh serum from the rabbit.



**A Nasal Sporozoön.**—JONATHAN WRIGHT (*New York Med. Jour.*, December 21, 1907) discusses, describes, and depicts the microscopic findings in a nasal sporozoön which he has studied from sections of a morbid growth sent to him by Dr. Ellett, of Memphis, which he believes to be identical with a growth of similar nature reported by Major Kinealy, of London (*Journal of Laryngology*, 1903). Wright names this parasitic protozoa, *Rhinosporidium kinealyi*, and states that it belongs to one of the most simple and primitive of the sporozoa.

**Wounds of the Optic Nerve in Operations on the Nose.**—ONODI (*Arch. internat. de laryng., d'otol., et de rhin.*, March to April, 1908) discusses the subject of wounds of the optic nerve produced by opening and emptying the posterior ethmoidal cells and the sphenoidal sinus, as well as in radical operations upon the frontal sinus and even in operations upon the septum of the nose. He attributes the result to either direct or indirect fracture of the optic canal.

**Morbid Growths of the Pharynx.**—MAGNE (*Rev. hebdomadaire de laryng., d'otol., et de Rhin*, April 4, 1908) reports a case of benign growth of the size of a pigeon egg in the inferior portion of the pharynx of a man, aged sixty-three years. Under light cocainization of its pedicle the growth was readily removed without hemorrhage by the electric incandescent snare. Examination of the tumor revealed it as a fibromyxoma. Magne gives a general summary of benign growths of the buccal and inferior portions of the pharynx.

**Direct Lateral Laryngoscopy and Oesophagoscopy.**—MOSHER (*Boston Med. and Surg. Jour.*, February 6, 1908) places the patient flat on the back with the head turned on the left cheek; and then, usually under ether anesthesia, he uses a bivalve speculum which he has devised and which is a combination of a tongue depressor and mouth gag, made for use upon the left side so that the operator can have his right hand for the manipulation of instruments. It exposes a larger field to vision than any other device hitherto employed, and utilizes the shortest anatomical route to the larynx and to the oesophagus.

**Bronchoscopy.**—A. INGALS (*Jour. Amer. Med. Assoc.*, March 7, 1908), in reporting the removal of a pin from the lung by upper bronchoscopy, refers to several severe electric shocks which he has received from the Kirstein light on his forehead while doing bronchoscopy and lighter shocks from the carrier of the small light passed through the tubes, and he has appreciated some danger in similar shocks to the patient. To prevent this he now wears rubber gloves and rubber overshoes and places his stool upon a rubber sheet. To guard the patient there are rubber castors on the table, but he thinks that we have all overlooked the possibility of the electric charge passing from the instruments through the patient and the assistants. He puts the question whether some of the hitherto inexplicable deaths from bronchoscopy may not have been due to galvanization of the vagus nerves; danger from which by instruments introduced for electrolysis of oesophageal strictures is well known to laryngologists; and in bronchoscopy the metal tube is quite as close to these nerves as the electrode would be in the electrolytic

procedure mentioned, and in unexpected ways the current may be passed through them. [It is for this reason that cautious laryngologists prefer to use the current from the battery rather than to utilize the street current when electric lights are to be passed into the interior of the body. J. S.-C.]

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**Papillomas of the Larynx in Young Infants.**—VAN DEN WILDENBERG (*Arch. internat. de laryng., d'otol., et de rhin.*, November and December, 1907) reports two cases of papillomas in infants, aged seventeen and eighteen months, respectively, in which the diagnosis was made by direct laryngoscopy with Killian's spatula under general anesthesia, with the head in the Rose position; the growths were removed by direct access with Killian's cutting forceps. In one case, however, cyanosis took place as a tumor was removed, and immediate tracheotomy was necessary. The next day remnants of the growth were removed by direct access as before. Both cases terminated favorably.

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**Sarcoma of the Mediastinum Invading the Thyroid Gland.**—SNYDER (*Jour. Amer. Med. Assoc.*, March 7, 1908) reports a tumor of the thyroid gland apparently connected with a mediastinal growth in a man, aged thirty-seven years, which was removed in extremis on account of the dyspnoea. The breathing, however, was only temporarily relieved and the patient died forty-five days after the operation. The autopsy revealed a large tumor occupying the entire mediastinum and adherent to all the neighboring organs except the left lung, while both lungs were completely collapsed and absolutely flat. The growth was found to be a round-cell sarcoma.

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## PATHOLOGY AND BACTERIOLOGY.

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UNDER THE CHARGE OF

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**Experimental Pleurisy.**—OPIE (*Jour. Exp. Med.*, 1907, ix, 391) has been able to produce quite an extensive exudate into the pleural cavity of dogs by injections into this cavity of small amounts of turpentine. The pleurisy which is thus produced resembles in many respects certain forms of this disease in man, and by percussing the chest of the dog it is readily possible to follow the rapid accumulation of the exudate during the acute stages as well as its gradual disappearance. The exudate is a coagulable fluid. The serous surfaces become covered by a layer of fibrin. The acute stage lasts about six days, while the fluid reaches its height in about three days. After six days the fluid has

generally disappeared, but the fibrin, although diminished in amount, is still present. At the end of two to three weeks the pleura regains its normal state except for the presence of a few fibrinous tags. The inflammation sometimes spreads from one pleural cavity to the other, so that if turpentine is injected into the right cavity fluid might accumulate in the left side.

The most important part of the investigation is concerned with the dissolution of the fibrin. It was found that the fibrin removed from the pleural cavity during the early stages of the inflammation, after the serum had been removed by thorough washing in salt solution, undergoes digestion when it is suspended in an alkaline or in an acid fluid, whereas the fibrin taken from the cavity during the latter stages of the process, for instance after five days, fails to digest in an alkaline medium, but digests readily in an acid medium. The digestion of the fibrin outside the body may be explained by the fact that cells which contain proteolytic enzymes are present in great numbers in the meshes of the fibrin. During the first part of the inflammation, polymorphonuclear leukocytes predominate, cells which contain leukoprotease, an enzyme acting best in an alkaline medium, while in the second stage the polymorphonuclear leukocytes have disappeared and the mononuclear cells are the elements which furnish the enzyme. This enzyme acts only in an acid medium.

That digestion of fibrin takes place within the pleural cavity during the inflammatory reaction was shown by the appearance of peptone and albumoses in the pleural fluid. These bodies were found in the pleural fluid after three days, and were present in less quantity at a later time. As is true of the blood serum, so the pleural fluid was found to inhibit the action of the enzymes contained in the leukocytes during all stages of the process. The exudate remains alkaline during the entire course of the inflammation, but its alkalinity is less than the blood and decreases slightly with the progress of the inflammation.

Since the acids, which *in vitro* favor the actions of the enzymes present during the latter stages of the inflammation, are not found in the body, it was thought possible that carbon-dioxide might bring this enzyme into action. This supposition was found to be true, for the presence of carbon-dioxide hastened very greatly the digestion of strips of fibrin suspended in salt solution. It was found, moreover, that carbon-dioxide would overcome the inhibitory effect which blood serum has upon these cellular enzymes, so that in the presence of small quantities of blood serum, carbon-dioxide causes greater enzymotic activity than in the presence of salt solution alone.

**The Combining Properties of the Opsonin of an Immune Serum.**—It is known, through the work of various observers, that the opsonin present in normal blood serum is a thermolabile body which is destroyed at a temperature of 55° C. Muir and Martin have shown in a previous communication that these thermolabile opsonins of normal serum may be removed from the serum by substances or combinations of substances which absorb serum complements. This work has been extended with the same result, so that the authors are prepared to group the normal thermolabile opsonins with the complements. Observations by many experimenters have been accumulating to show that in immune sera the substance which causes phagocytosis of bacteria or red blood corpuscles

is thermostabile and resists a temperature of 55° C. for one hour. MUIR and MARTIN, (*Proceedings of the Royal Society*, B, 1907, lxxix, 187) have taken up the question of the opsonins of immune sera and have studied these bodies in the sera of animals immunized against *Staphylococcus aureus*. They find that only a part of the opsonins of this immune serum is destroyed by a temperature of 55° C. After treating the serum with complement-absorbing substances the power of the serum to phagocyte staphylococci is only partly lost. Since both heat and complement-absorbing substance remove approximately the same amount of opsonin, Muir and Martin conclude that this portion is the normal opsonin and that the remaining thermostabile portion is a different substance, namely, the opsonin of immune serum. These immune opsonins were found, moreover, to have a certain degree of specificity. Whereas a great variety of bacteria removed large quantities of the opsonin for *Staphylococcus aureus* from normal serum, they removed very little of the opsonin for this particular organism from immune serum. *Staphylococcus aureus* will, on the other hand, absorb practically all the opsonin from immune serum. The opsonin of immune serum acts in a distinctly different manner from the opsonin of normal serum. While the normal opsonin is of the nature of the complement, the immune opsonin resembles the constitution of an agglutinin or of an immune body.

**Lipase in the Blood.**—It has been shown by Neuberg, Reicher, and others that bactericidal and antitoxic sera contain a ferment which is capable of splitting fats; and PRYBRAM (*Zentralbl. f. inn. Med.*, 1908, xxix, 81), with the work of these investigators in mind, undertook some experiments to determine whether a lipolytic ferment could be demonstrated in the sera of patients suffering from various diseases. The technique consisted in allowing blood serum to remain in contact with olive oil. The tube containing this mixture was placed in the thermostat at 36° C., and another tube kept as a control in the ice chest. The mixtures were titrated with  $\frac{1}{10}$  normal sodium hydrate; phenolphthalein was used as an indicator. The presence of acid in the mixture kept in the thermostat showed that the olive oil had been partially converted into fatty acid. The examination of 21 cases showed that lipase was present only in the sera of those patients who had a high fever. In one case lipase could be demonstrated in the serum after the patient was exposed to x-rays, and therefore, to see if the x-rays had any influence in giving rise to this ferment in the blood serum, rabbits were exposed to the action of the x-rays and their serum was tested before and after treatment. These last experiments yielded varying results, and it could not be determined what action, if any, the x-rays played.

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All communications should be addressed to—

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**PATHOLOGY AND BACTERIOLOGY.**

UNDER THE CHARGE OF

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AND

G. CANBY ROBINSON, M.D.

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THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES.

AUGUST, 1908.

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ORIGINAL ARTICLES.

**SPLENIC ANEMIA, SPLENECTOMY, AND RECOVERY.<sup>1</sup>**

WITH STUDIES OF THE BLOOD COVERING A PERIOD OF SEVEN YEARS.

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THE fact that the patient, whose case I report herewith, has been subjected to a careful study for a long period of time, four years before and three years following the operation of splenectomy, makes the case worthy of record. During this whole period of seven years a large number of blood examinations have been made most accurately for me by one man, Dr. W. Estell Lee, chief resident physician of the Pennsylvania Hospital, Philadelphia, to whom I wish to give credit. The question of the personal equation, which often interferes with the accuracy of work, is thus reduced to a minimum.

J. M., a male, was seventeen years of age at the time of operation in 1904. He had been under my professional care since infancy, but came under particular observation in 1900 at which time the first enlargement of the spleen was detected. Shortly after his birth, which was a most difficult one, his mother was found to be suffering from nephritis, which had affected other members of her family. Some years later, after another pregnancy, she died uræmic. The patient's father is of a very nervous temperament, but otherwise healthy. At the age of two years, the patient was enormously fat, but seemed to be perfectly healthy. His family was living near the

<sup>1</sup> Read at a meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1908.

Schuylkill River in a somewhat malarial neighborhood, and the child had several attacks of indisposition with fever, during which the probability of malaria was considered, but at no time could the plasmodium be discovered in his blood. In 1900, when thirteen years of age, he was found wanting in tone and quite pallid, with a decided bronchitis. Examination of his spleen showed it to be slightly enlarged. Quinine, iron, and arsenic were administered with apparent benefit.

In March, 1901, an examination of his blood showed 5,260,000 red cells, 5460 leukocytes, and 74 per cent. of hemoglobin. No plasmodia were discovered; there was marked poikilocytosis. The organs of the chest and abdomen appeared normal. The boy was a very large eater, with constipation alternating with diarrhoea. His abdomen was large, and had always been so, and he had occasional attacks of indigestion. At this time, curiously, no enlargement of the spleen could be detected, although palpation and percussion caused pain.

In May, 1902, an examination of his blood showed red blood cells, 4,688,000; leukocytes, 8000, and hemoglobin, 69 per cent. No malarial organisms were found, and the poikilocytosis, though slight, persisted. In October of this year, after a summer holiday at Digby, Nova Scotia, his spleen was found to be enormously enlarged, extending two and one-half inches below the lower border of the ribs. His blood showed red cells, 5,400,000; leukocytes, 4800, and hemoglobin 72 per cent. He looked quite pale, was languid and disinclined to play, and his bowels were capricious. He was growing considerably taller and heavier, but not keeping up his strength. His weight was ninety-six and three-quarter pounds. By the spring of 1903 he had made a decided improvement. His red cells were 5,420,000, his leukocytes 6200, and his hemoglobin 84 per cent; all poikilocytosis had disappeared. His color was better and the spleen appeared to have diminished in size and was absolutely painless to percussion and palpation.

In the autumn of 1903 he returned from Europe looking well. While there, several physicians were consulted, but no light was shed upon the diagnosis or treatment. He now weighed 111 pounds, which rapidly, on his return, increased to 119½. The splenic area remained the same. Notwithstanding his improved appearance, his red cells had fallen to 4,340,000, and his hemoglobin to 69 per cent.

By the spring of 1904 his appearance had further improved, his red cells had risen to 5,020,000, and his hemoglobin to 90 per cent. He still was given to overeating, ate too fast, and as a consequence suffered from occasional indigestion.

On the night of May 22, 1904, after an unusually hearty meal, he felt nauseated and vomited a little blood, but there was no melena or diarrhoea. In the morning he felt sufficiently well to go to school.

On the morning of the 25th he awoke feeling oppressed, but

not nauseated, and had an explosive attack of vomiting of blood; the amount vomited was very large, one of the family remarking that the bathroom looked like a "shambles." During the day this vomiting of blood was twice repeated, and later in the day he had a large tarry evacuation.

When seen in the evening he was ghastly pale and had very violent pain to the right of the ensiform cartilage, about over the notch of the liver. His abdomen was distended, but there was no rigidity of the recti muscles. Palpation over the region of the gall-bladder elicited decided pain. The stomach was greatly distended, the greater curvature extending nearly to the horizontal line of the navel.



FIG. 1

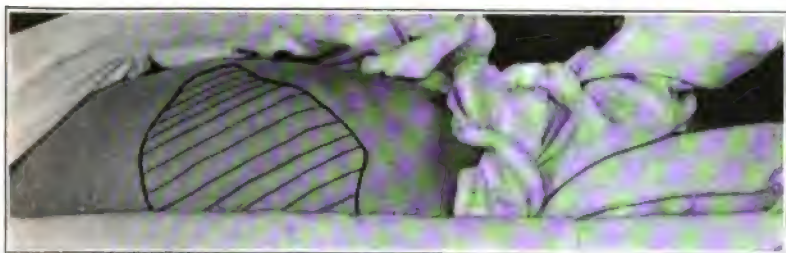


FIG. 2

FIGS. 1 and 2.—Area of splenic dulness as marked on the patient shortly before operation.

His temperature was 102° F. During the night he had two large tarry evacuations. He was at once removed to the Pennsylvania Hospital, where he had, during the next night, several bloody evacuations. His hemoglobin was now only 30 per cent. and his red cells 2,200,000. By the next morning his temperature had returned to normal and his stomach had returned to its normal position. The area of the splenic dulness had decreased decidedly (Figs. 1, 2, and 3). On the 26th the hemoglobin had fallen to 25 per cent., and brighter blood began to be passed with the stools.

On account of the previous symptoms pointing to gastric indigestion and the continuance of the bleeding from the bowel, the question of gastric or duodenal ulcer was considered. A consultation was

held with Drs. LeConte and Harte, and the operation of posterior gastro-enterostomy was decided upon and performed by Dr. Harte. During the operation no sign of ulcer was detected either in the stomach or bowel. The patient rallied slowly from the operation, during which two quarts of normal salt were used by transfusion.

During the next two days he had fourteen bloody evacuations, losing in all thirty-six ounces of blood, but by the 29th practically all bleeding had ceased. On May 31 and June 1 his hemoglobin percentage was only 18.

He made an uneventful recovery from the gastro-enterostomy, all stitches being removed by the end of the second week, at which time

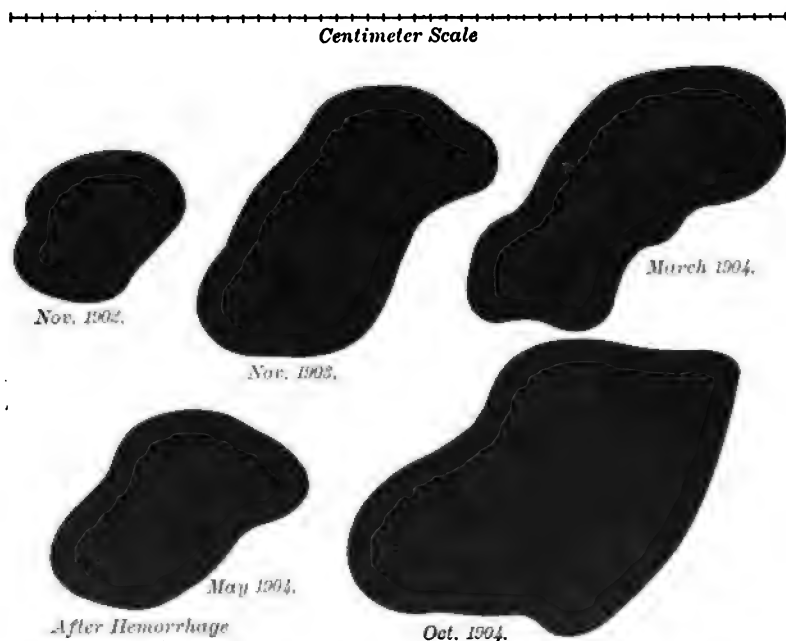


FIG. 3.—Variations in the size of spleen as shown by percussion and palpation.

his spleen was found to extend three inches below the margin of the ribs in the midaxillary line.

Shortly after this his liver enlarged decidedly, his abdomen became distended, and considerable ascites appeared. His evacuations were now frequent and liquid, but not bloody. By July 12 he was considered to have improved sufficiently to be sent to Atlantic City to recuperate. Occasional bloody streaks appeared in his evacuations until the middle of August. By September he was feeling well, had a good appetite and no trouble with digestion, and was able to walk without fatigue. His hemoglobin was 52 per cent., his red cells numbered 3,400,000 and showed slight poikilocytosis,

and his leukocytes were 4200. By October, 1904, his spleen had increased much in size (Fig. 3). He had gained four pounds in weight and his blood had improved slightly, showing a hemoglobin percentage of 54, and a red cell count of 4,200,000. He was having, on an average, six bowel movements, slightly streaked with blood, every day, but no true hemorrhage. The large spleen appeared to be freely movable, and examination of the other organs was negative.

He was again admitted into the Pennsylvania Hospital, and the operation of splenectomy was decided upon. The patient felt no inconvenience at any time from the previous operation of gastro-enterostomy, although in the light of the further study of the case and the diagnosis of chronic splenic anemia, which it was feared was in the terminal stage, or Banti's disease, we regretted having performed it. It is true the hemorrhage lessened after the operation, and the thought has since arisen whether possibly the adhesions which must have formed had not really had the effect of an accidental Talma's operation, forming an anastomosis between the internal veins and those of the abdominal wall, thus relieving the venous congestion and really improving his condition. This result occurred after gastro-enterostomy in a case of profuse gastric hemorrhage seen by me in consultation with Dr. Wm. J. Taylor, of Philadelphia, and later reported by him.<sup>2</sup> Could it be possible that the lessened motions of the stomach, consequent upon the operation, had been effective in diminishing the venous oozing? for after the fourth day very little blood was passed by the bowel.

The operation of splenectomy was performed by Dr. Harte on October 14, 1904. The spleen was found tightly adherent. Silk ligatures were used for the many adhesions and for the splenic vessels. Gauze drainage was used.

This case, although not heretofore reported by Dr. Harte or myself, has been listed as a successful case of splenectomy by Dr. G. E. Armstrong,<sup>3</sup> of Montreal, Canada, and also by Dr. Gaston Torrance,<sup>4</sup> of Birmingham, Alabama. This fact is referred to here for accuracy, in order that it may be seen that these two reports and mine all refer to one and the same case.

The patient reacted fairly comfortably, but in six days a slight pleural effusion, with impairment of expansion of the posterior portions of the left lung, was discovered. A week later pericarditis supervened, but from this and the pleural effusion, and from a secondary abscess in the wound, which was opened on September 9, and from which three ounces of pus was discharged, he recovered perfectly. A sinus remained for weeks subsequently, and all the silk

<sup>2</sup> Trans. Coll. of Phys., Philadelphia, 1906.

<sup>3</sup> Brit. Med. Jour., November 10, 1906, Case No. 25.

<sup>4</sup> Charlotte (Alabama) Medical Journal, 1907, Case XXXI.

sutures were discharged one by one until 23 were collected, when the sinus closed entirely (the end of October, 1905), and has since given no trouble. At this time he looked well, weighed 126 pounds (clothed), had a good appetite, and never felt better in his life. He was able to take exercise freely without any sense of strain.

By the next year he again had some sense of indigestion, which was undoubtedly due to indiscretions in diet. At no time has there been any pigmentation of the skin or enlargement of the thyroid or of the lymphatic glands. The patient now, in 1908, seems to be in perfect health, although, as might be expected, indiscretion in diet causes some distress and diarrhoea. He weighs over 130 pounds, he is very active, and takes exercise, swimming, etc., with perfect comfort. He has had no further hemorrhage.

As a proof of his occasional indiscretion in diet, he has been known, since the operation, to eat, on a wager, twelve ears of corn at one sitting, and not suffer seriously in consequence, except for a diarrhoea which yielded to appropriate treatment. An inveterate acne vulgaris appeared shortly after the operation and still remains, notwithstanding all efforts to relieve it.

The blood charts (Figs. 4, 5, and 6) show: (1) The percentage of hemoglobin, and the red blood cells per cubic millimeter from March 16, 1901, to February 20, 1908. (2) The total leukocyte count for the same period; and the polymorphonuclear leukocytes, the large mononuclear leukocytes, and the lymphocytes, all per cubic millimeter, for two periods: May 5, 1904, to July 22, 1904, and from October 14, 1904, to February 20, 1908. (3) The eosinophiles and basophiles per cubic millimeter also for two periods: May 28, 1904, to July 22, 1904 (the gastro-enterostomy period), and from October 14, 1904 (the splenectomy period), to February 20, 1908.

The continuous tracings on the charts represent the period when but a day or so elapsed between the examinations, while the isolated records represent the examinations which have been made at considerably longer intervals. To join both of these records with a continuous tracing would give an erroneous impression as to time relationship. The total number of the elements of the blood have been calculated for each cubic millimeter rather than recording the percentages.

In examining Fig. 4, it is seen how profuse the hemorrhage was, as the hemoglobin fell from 90 per cent., where it was but a short time before the loss of blood, to 18 per cent., which low point was reached a few days subsequently; this and the subsequent rise to health is represented by the continuous line and by the isolated records. The broken line shows the red blood cells per cubic millimeter.

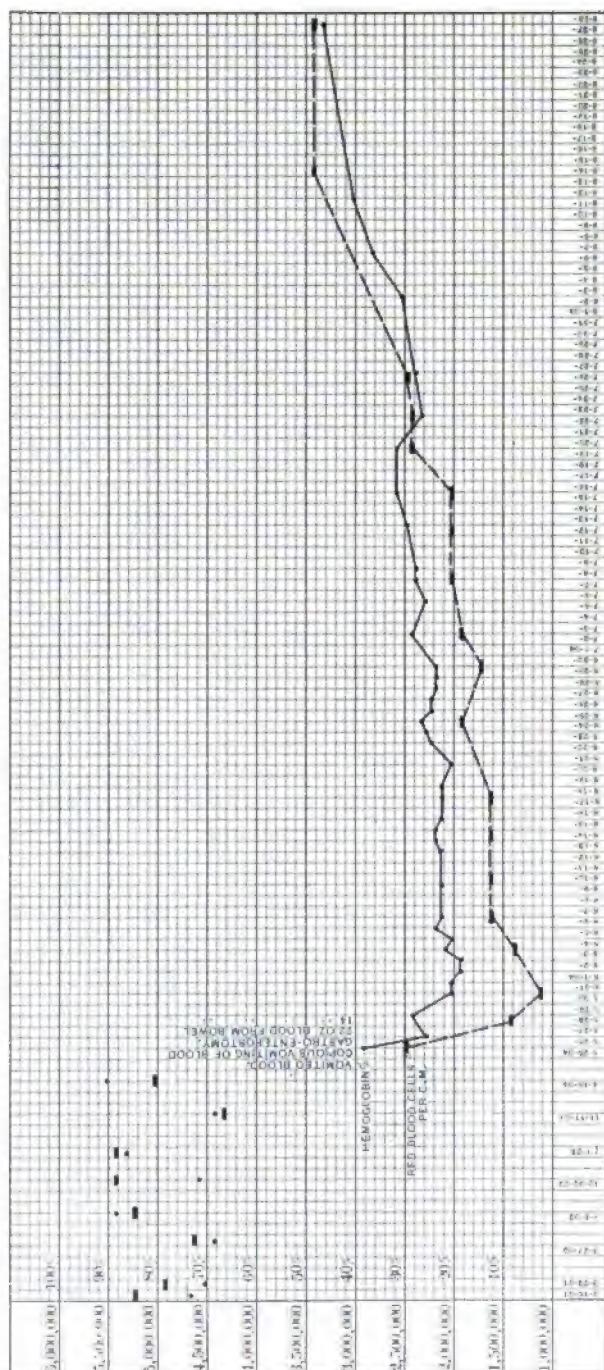
In Fig. 5 two periods of leukocytosis are seen, the first being a posthemorrhagic leukocytosis in May, 1904, and the second period

corresponding with the time of removal of the spleen. A rapid rise to over 10,000 per cubic millimeter occurred in three days, this rise being evidently largely due to the inflammatory complications which followed the operation: pleural effusion, pericarditis, and the abscess in the wound; this continued until 24,000 leukocytes per cubic millimeter was reached, after which the count rapidly fell, so that within one month after the operation it averaged 10,000 per cubic millimeter; this average has remained until the present time, considerably higher than it was before the violent vomiting of blood at which time the count averaged about 6000 per cubic millimeter, and very much higher than the low quiescent period, between the two operations, when it averaged 4000 per cubic millimeter. As all apparent cause of leukocytosis is absent, unless it might be the pronounced acne, it is difficult to disassociate it from the removal of the spleen and the consequent compensatory reaction of the bone marrow. Ehrlich and others distinctly assert that leukocytosis is purely a function of the bone marrow. The polymorphonuclear count follows very closely in character the tracing of the total leukocytes, and shows a marked increase over normal immediately after the splenectomy period and during the subsequent inflammatory complications, but it soon falls to normal. The lymphocytes show a moderate irregular rise at two periods: at two weeks and at one and a half years after the removal of the spleen, and even here the normal count of from 20 to 25 per cent. of the total leukocytes was barely reached.

Fig. 6 is most interesting and shows the marked eosinophilia which occurred immediately after the splenectomy. The large number of eosinophile records which were made previous to the operation also renders this chart valuable, as in most cases of splenectomy but few records have been taken previous to the operation. This absence of pre-operative eosinophilia rather points to the fact that the functions of the spleen were not entirely abrogated by disease, else according to Kurloff's law of the secondary reaction of the bone marrow, they would have been increased.

During June and July the eosinophile count varied from 10 to 100 per cubic millimeter, with an average of 50, during which time the total leukocyte count fell from 16,600 to 1200 per cubic millimeter. There is but little change in the eosinophile count for this period, but if the total leukocyte count is examined it will be seen that a very great change in the percentage of the former occurs.

The method of tabulating the actual count of the blood elements per cubic millimeter is preferable to registering the percentage, as the latter, as has just been stated, may change decidedly without correspondingly altering the actual count. The high eosinophile record of 1800, on October 31, 1904, out of a total leukocyte count of 16,000 is only equivalent to 11.2 per cent., while the much lower records of 630 eosinophiles, on November 3, 1904, out of a total leukocyte





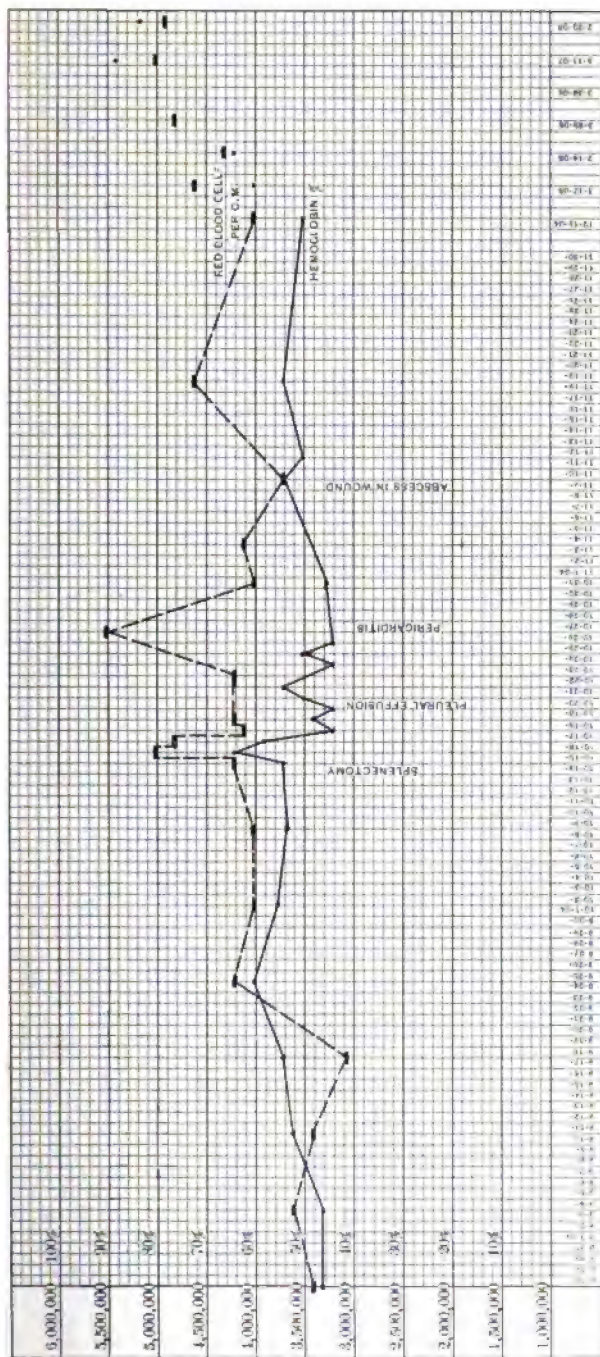
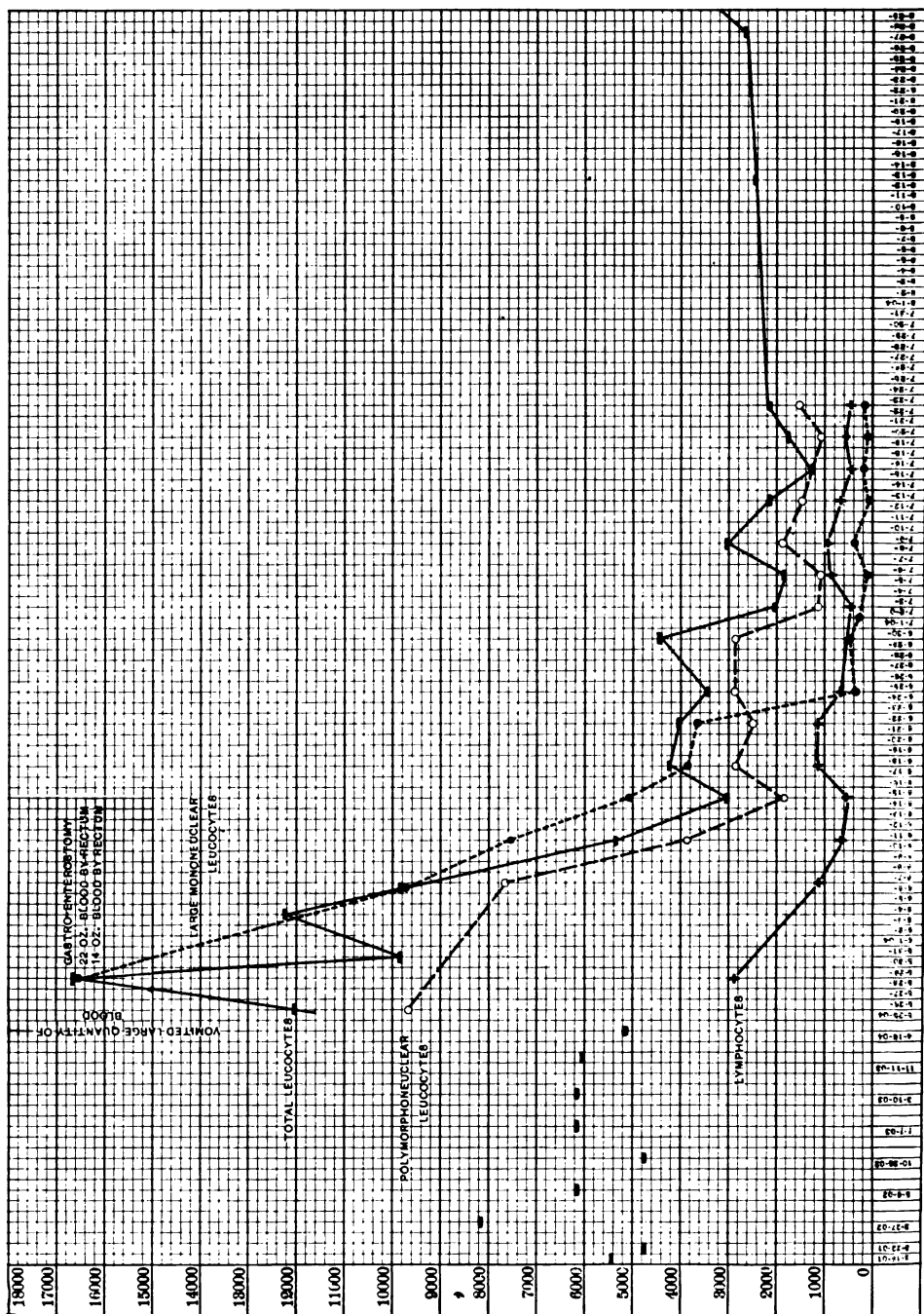


FIG. 4.—Percentage of hemoglobin and the red-blood cells per cubic millimeter, from March 16, 1901, to February 20, 1908.



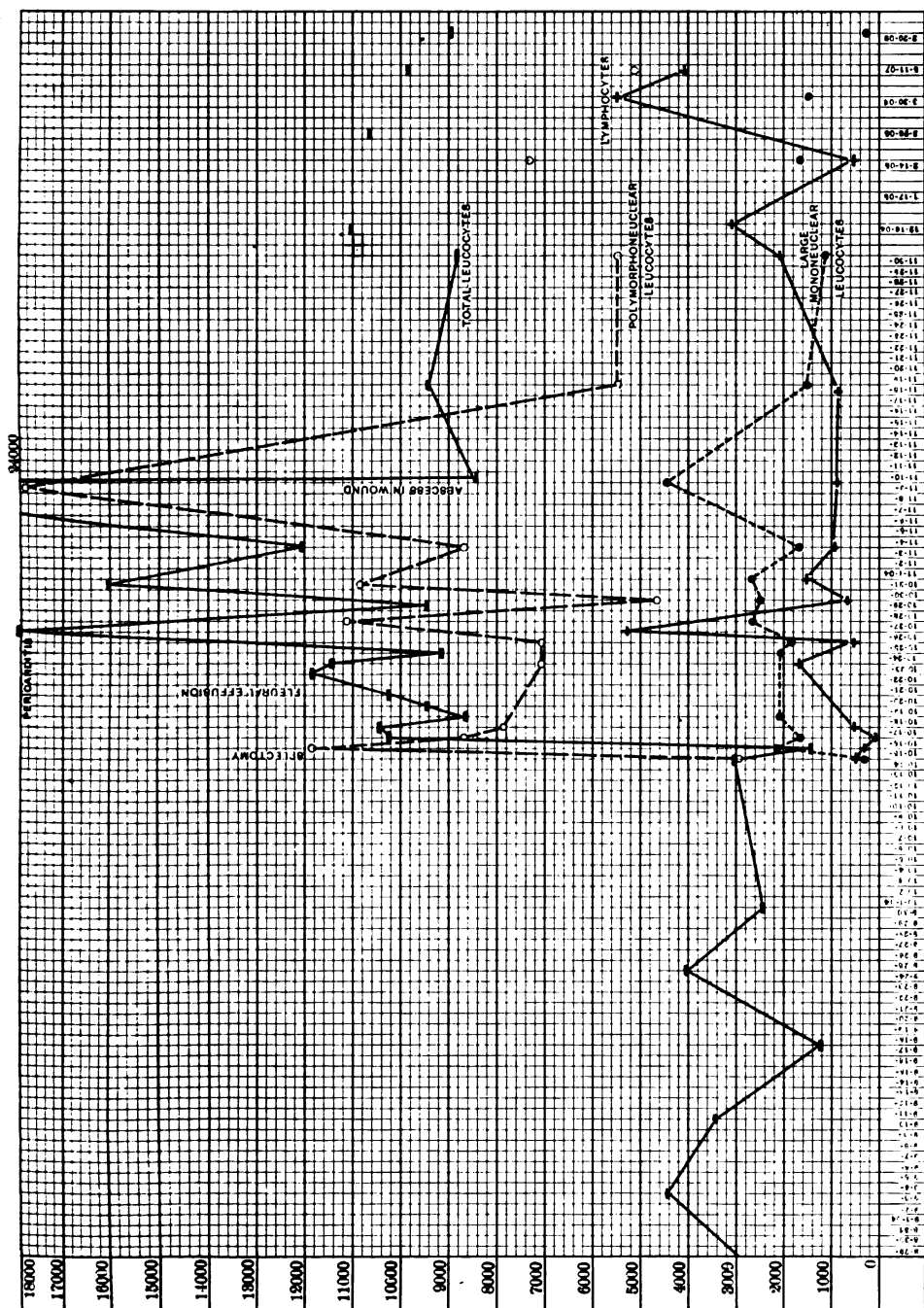


Fig. 5.—Total leukocytes, polymorphonuclear leukocytes, large mononuclear leukocytes, and lymphocytes per cubic millimeter, at the dates indicated on

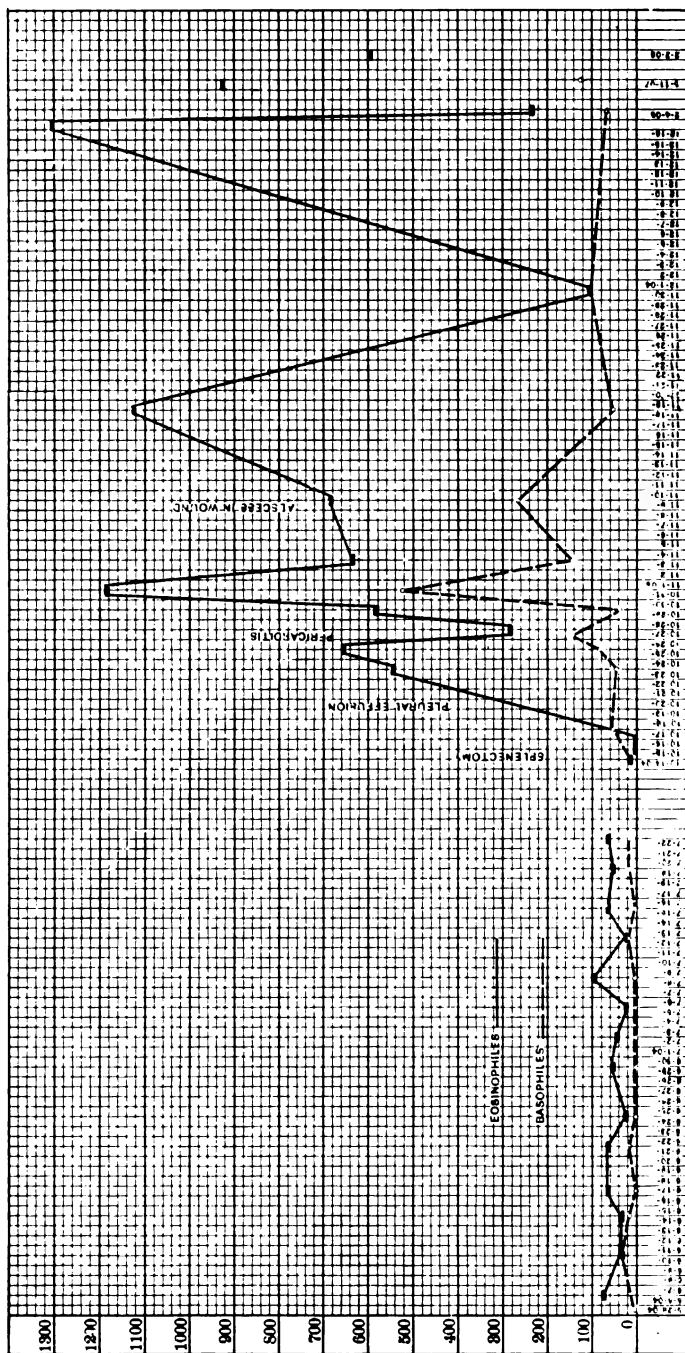


Fig. 6.—Eosinophiles and basophiles per cubic millimeter, at the dates indicated on the margin.

count of 13,000, and of 670 on November 8, 1904, out of a total leukocyte count of 24,000, represents 4.8 per cent. and 2.8 per cent., respectively, which would lead one to an erroneous opinion as to their actual numbers. Two depressions in the tracing correspond to the time of the pericarditis and the abscess formation. The two very low points, 100 and 203, respectively, per cubic millimeter, do not correspond with any recognizable changes in the patient's physical condition, nor with anything unusual in the tracings on the other charts.

The sudden postoperative eosinophilia does not agree with the statements of Kurloff, or of Hartmann and Vaquez, who state that eosinophilia is a late manifestation after this operation, and is due, as previously stated, to the secondary reaction of the bone marrow, the so-called compensatory eosinophilia.

In the case of splenectomy reported by Stengel<sup>6</sup> 7.8 per cent. of eosinophiles were found on the day before the operation, but as he neither mentions the number per cubic millimeter nor the total number of leukocytes, the record cannot be compared with my tracing. It is, however, a positive eosinophilia antedating the operation. An immediate drop to 0.2 per cent. occurred, and then a rise on the fourth day to 10.5 per cent., or a total of 1335 per cubic millimeter; but in this case, as in mine, the record was probably modified by a serious postoperative complication; in Stengel's case, pneumonia.

Kurloff, in his studies on splenectomized guinea-pigs, quoted by Ehrlich, reaches the conclusion that a lymphocytosis "occurs so constantly in the course of the first year after the operation as to constitute a characteristic of the absence of the spleen," and that this lymphocytosis "in the majority of cases retrogrades during the course of the first year even to a condition in which a less number of lymphocytes than normal is produced." This condition does not obtain in the present case, as may be seen in Chart II; neither did it occur in Stengel's case.

Hartmann and Vaquez, quoted by Ehrlich, conclude that splenectomy causes: (1) A slight postoperative increase of the red blood corpuscles, and a genuine, though very transitory, acute hyperleukocytosis. (2) A primary decrease of hemoglobin, which gradually rises again to normal. (3) After four to eight weeks a lymphocytosis of varying duration. (4) A moderate eosinophilia occurring late, after many months.

The correct understanding of the blood changes after splenectomy in man can only be attained when splenectomy is performed for injury to that organ in a previously healthy individual and when the wound heals without any complications supervening, a condition probably impossible to attain. This study, however, enhances our

<sup>6</sup> Trans. Assoc. Amer. Physicians, 1904.

knowledge of the blood and the changes occurring in it after splenectomy, and justifies the report.

The size of the spleen may be seen in the photographs taken shortly before operation, the splenic area being traced on the patient's body (Figs. 1, 2, and 3), and in the photograph of the removed spleen (Fig. 7). Naturally the splenic area, as mapped out by palpation and percussion while the organ was still in the patient and full of blood, would make the spleen appear larger than is seen after removal. Fig. 3 shows the variations in the apparent size of the spleen as thus mapped out, as well as the marked effect of the severe hemorrhage in May, 1904.

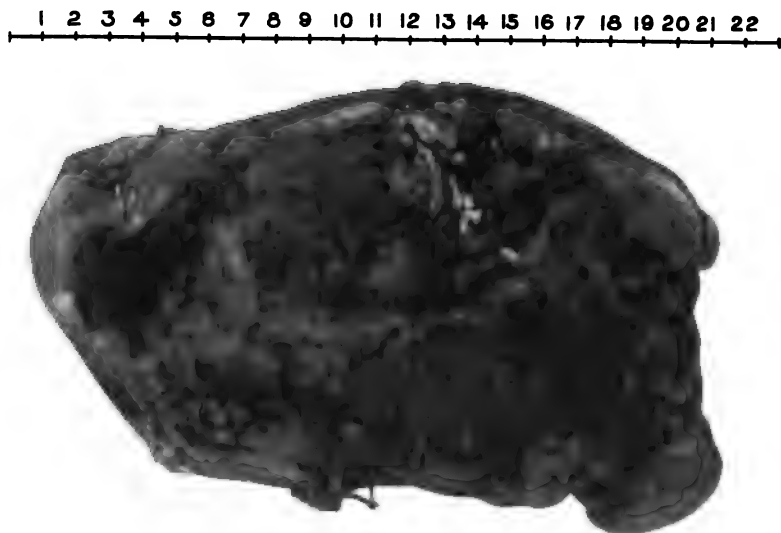


FIG. 7.—Photograph of the spleen immediately after removal. (The measurements are in centimeters.)

The unusual number of ligatures that were required, 23 in all, prove how great was the dilatation of the splenic veins. The application of these ligatures produced no appreciable effect upon the venous circulation, as might have been imagined, but all blood at once ceased to appear in the evacuations, which tends to prove that the spleen is not merely passive in this disease. The enlargement of the liver, so frequently seen, existed for a short time only, about two weeks after the gastro-enterostomy, was accompanied by ascites, and then entirely subsided, and was absent at the operation for splenectomy.

Dr. Warfield T. Longcope, director of the Ayer Clinical Laboratory of the Pennsylvania Hospital, reports as follows concerning the examination of the spleen:

"The spleen is of very great size. It weighs 790 grams and



measures 20 x 13 x 7 cm. It is quite firm in consistency and has a rubbery or leathery feel. It is quite irregular, and there are three fairly deep notches on the upper margin. A great many adhesions cover the capsule, and on the superior surface two depressed white thickened areas are seen. The largest measures 5 cm. and is situated in the posterior portion. The other measures 4 cm. in diameter and is situated in the inferior anterior portion. The color is rather a pale red. On section the cut surface is smooth, slippery, and rather dry. The pulp is firm and of a homogeneous light red color. The Malpighian bodies are very small or invisible. Trabeculae are very white, prominent, and are much increased in number and size. The vessels at the hilum are clear.

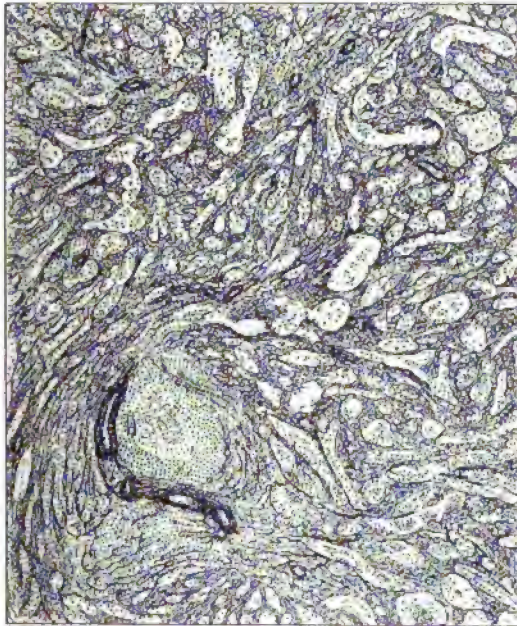


FIG. 8.—Microscopic appearances of the spleen.

"Smears are made from the freshly cut surface of the spleen and stained in Wright's stain. Most of the cells are red blood corpuscles. A few normoblasts are seen. The white cells are principally small lymphocytes. Moderate numbers of large lymphocytes are seen and several much larger cells which are apparently endothelioid cells. Fair numbers of polymorphonuclear leukocytes are met with. Quite a large proportion have eosinophilic granules. No phagocytic cells or red-blood-corpuscle-carrying cells. No cellular inclusions. No pigment.

"Sections are made through various portions of the organ. They

all have about the same appearance (Fig. 8). The capsule is very much thickened and is composed chiefly of hyaline connective tissue. To it are attached irregular projections of fat and connective tissue. Throughout the section there is a very extensive increase in connective tissue, both in the trabeculae and in the pulp. The organ contains comparatively little blood. The walls of the venous spaces are greatly thickened by a growth of rather cellular connective tissue. In Mallory's connective tissue stain the walls are seen to be made up of a reticulated fibrous tissue. The venous spaces are small. Besides red blood cells they contain a few polymorphonuclear leukocytes, many small round cells, and an occasional large endothelioid cell. Very rarely a red-blood-corpuscle-carrying cell is seen. The cells in the walls of the sinuses are principally connective tissue cells. No uninuclear or multinuclear giant cells are seen. Very few eosinophiles are seen in sections.

"The Malpighian bodies are quite scarce. Many of them are very small. The reticulum beneath the cells is thickened and the follicle is overgrown with connective tissue. Others appear unusually large and show compensatory hypertrophy. They are quite regular. The middle of the follicle is composed of a large germinal centre filled with large irregular pale cells of epithelioid type. The margin is quite regular and is bordered by a narrow dense zone of small lymphocytes. Beyond this is a wider, paler zone of cells, chiefly small lymphocytes, fairly well separated and mixed with a few large lymphocytes and epithelioid cells. The boundary zone is regular and definite. The reticulum is not thickened except in a few instances about the outer border. No pigment is seen. There are a few small areas of blood mixed with fibrin. The connective tissue about the vessels is much increased, but the intima of the blood-vessels is delicate. Taken as a whole, the spleen shows an extreme grade of thickening of the walls of the venous spaces with a diffuse increase in rather cellular connective tissue. Many of the Malpighian bodies are atrophied, though a few are exceedingly large with active proliferating germinal centres.

"Diagnosis: Chronic perisplenitis and interstitial splenitis."

## CLINICAL NOTES ON LARYNGEAL TUBERCULOSIS.<sup>1</sup>

BY BEVERLEY ROBINSON, M.D.,

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It seems to me it may be of interest to record some personal observations and experience about tuberculosis as it appears in the

<sup>1</sup> Read at a meeting of the New York Academy of Medicine, January 16, 1908.



larynx. I shall also emphasize certain facts pertaining to its management and treatment which I regard as very important. For many years I had extensive opportunities of seeing and treating this disease. Latterly my patients are fewer, but I have tried to keep track of recent methods, and while in a few instances I believe real advances have been made as to our knowledge of laryngeal tuberculosis, I am also convinced that a return with newer lights to older practice is really the important asset of many among us.

In a fair proportion of cases of pulmonary tuberculosis we have, as we all know, laryngeal complications. These complications are more frequent among men than women, and are reasonably explained by different occupations in which the larynx is exposed to more irritating influences. One fact which seems to me of great importance is the ignoring of the larynx in far too many cases of suspected or confirmed pulmonary tuberculosis. In the first category a laryngeal examination by means of the laryngoscope may frequently fix a diagnosis which is very obscure prior to it. Nor is this examination always less important simply because there are few or no laryngeal symptoms. The voice may be almost, if not entirely, normal at times, and yet there may be inactivity or slight paresis of one or both vocal cords; or there may be marked localized anemia;<sup>2</sup> or there may be slight congestion of one or both vocal cords in a limited area; or the arytenoids may be slightly infiltrated, and likewise the interarytenoid commissure. Yet these appearances are already suspicious; indeed, with a certain history they are more characteristic even than a little prolongation or harshness of the expiratory murmur at the apex of the lung, or an indefinite dulness, which is often nothing more than the result of the percussion note elicited by a finger from a relaxed or possibly corpulent chest wall.

Again, in the very frequent cases of huskiness or hoarseness of voice, more or less remittent or intermittent, and usually considered and treated as a slight cold, or catarrhal inflammation of the larynx, do not the appearances under the laryngoscope enable us often to differentiate properly what is and what is not a first stage of laryngeal tuberculosis? In the former instance the redness is far more general; in the latter it is localized to a limited portion of the vocal cords, the ventricular bands, or other portion of the larynx.

In the cases in which there is marked hoarseness, some intralaryngeal discomfort or pain, or dysphagia even if only moderate, a laryngeal examination of course should be properly made. In every case, and emphatically in all young adults, in whom a cold or cough has unduly persisted despite rational treatment, or whenever the causation seems in any way obscure, we should invariably

<sup>2</sup> Dr. Herbert Maxon King, physician-in-chief at the Loomis Sanitarium, Liberty, New York, writes: "A pallor of the larynx is very significant and often an early sign" of pulmonary tuberculosis. *New York Med. Record*, December 14, 1907, p. 977.

insist upon a laryngeal examination. Time and time again I have seen an ulceration of the vocal cord, of the arytenoid cartilage or commissure, of the arytenoid folds, and even of the epiglottis itself, when the laryngeal symptoms were not unduly pronounced. And these cases, again, occur, although perhaps infrequently, when the intrapulmonary condition is not perfectly clear and when no tubercle bacilli have yet been discovered in the sputum.

When we have noted any one of the preceding conditions, besides confirming our diagnosis as to the presence of pulmonary tuberculosis in the very great majority of cases, is it otherwise valuable to the patient and to us? Certainly. In the first place, when the laryngeal condition is only catarrhal, will not proper management and treatment prevent it from becoming tuberculous? It is only necessary, as I believe, in some instances, for the mucous membrane to lose its epithelial covering, or to become in the slightest degree abraded, to have a portal of entry for the infecting germ. When the case is one of manifest laryngeal tuberculosis at its initial stage, may we not by judicious management prevent the local disease from extending and getting, sooner or later, beyond our means of control or arrest? To these questions I answer unreservedly, we can occasionally, I believe.

Of course, I admit, and we all should admit, that the general treatment which is wisest and best for the intrapulmonary tuberculosis is also most judicious, even if there be a laryngeal complication. But, on the other hand, there are certain clear-cut indications of management and treatment which proceed directly from the localization. The importance of this treatment must be admitted when we state how great the added suffering often is of the patient who has advanced ulcerative disease of the larynx with the accompanying infiltration or œdema of certain parts, and with the loss of vocal function which is thus occasioned. But this is as nothing to the dysphagia, often allied with increased dyspnoea from obstruction, which makes every act of swallowing a torture. Even when the pain of swallowing has been lessened by anodynes, or position, distressing paroxysms of cough are not obviated by reason of solid particles or fluids penetrating into the larynx.

In the way of protective and curative treatment, what should be insisted upon? In my judgment two things, essentially: (1) rest for the larynx, and (2) inhalations. Upon the great necessity of rest to the larynx, Sir Felix Simon, of London, and after him I<sup>3</sup> insisted many years ago. For several years past, many indeed, the importance of this matter lay dormant, as it were, or, at all events, was not insisted upon as it should be. Again it is to the fore, and during the past year or two, in more than one book and in several journal articles it is amplified and accentuated. In some

<sup>3</sup> Proc. Amer. Laryngol. Assoc., 1880.

sanitaria for tuberculous patients, when the larynx is at all affected, partial or complete silence is insisted upon. As far as may be, everything is written with slate and pencil or upon a writing pad, and the spoken word is not permitted. Of course, we cannot get complete rest for the larynx in this way because every drawn breath, every paroxysm of cough, every act of deglutition causes laryngeal movement, and alas, at times, discomfort or pain; but we lessen movement as far as possible, and by so doing we afford the patient a better chance of cure.

Are the results such as to justify our hopes and expectations? Frequently they are. Congestion and infiltration have greatly diminished or wholly disappeared. Ulcerations, when limited, have entirely healed. And this has come about not only when the general health and intrapulmonary condition have both notably improved, but also when the latter have remained stationary or deteriorated.

There is nothing new about the great value of the principle of rest in many, very many diseased conditions—both medical and surgical—but, except for a broken bone or diseased joint, nowhere else does it seem more useful, in some instances, than in diseases of the larynx. To Hilton, above other writers, we owe a great debt for wise insistence upon this very important fact of the great utility of rest in the management and treatment of many accidents and diseases—both acute and chronic.

In a few instances it has been noted by myself and others that when tracheotomy had been performed for laryngeal tuberculosis, with marked and distressing stenosis, the condition of the diseased parts were notably and favorably modified apparently or, indeed, obviously, by the rest to the larynx thus afforded.<sup>4</sup>

Formerly, in all instances of laryngeal tuberculosis at the initial stage, I made use of atomized solutions followed or not by some pigment locally. Frequently, and preferably, this pigment was tincture of iron perchloride combined with glycerin and water. At a later period, and when there was pronounced infiltration with œdema of the arytenoids, arytenoid folds, or epiglottis, with notable amount of mucus or mucopus covering the posterior portion of the larynx, or filling and obscuring its interior, the frequent use of an alkaline, carbolic spray by means of Sass' tubes appeared to be the best preparatory cleansing application before the use of iron, zinc, tannin, nitrate of silver, etc. These latter applications at this stage were rarely used except of moderate strength, or well diluted, for the reason that otherwise they sometimes caused distressing spasm. And later there was occasionally local and increased laryngeal uneasiness for a time and no subsequent evident improvement in the local condition. Whenever ulceration appeared, was localized,

<sup>4</sup> Beverley Robinson. Tracheotomy in Ulcerative Phthisical Laryngitis, AMER. JOUR. MED. SCI., April, 1879.

and could be readily seen, attempts were made to reach it directly with somewhat stronger pigments by means of a swab, brush, or curved probe on which nitrate of silver had been fused or chromic acid fixed. Rarely, if ever, have I had occasion to make use of the galvanic cautery to infiltration, thickening, swelling, or ulceration. Whenever there was notable excrescence of tissue, more particularly in the interarytenoid fold, I have either made use of the stronger applications referred to, or, as a preliminary measure, employed the tube or other suitable forceps to reduce the redundancy of tissue. In no instance have I attempted to make use of submucous injections in the larynx or the trachea. They never appealed to me strongly as a remedial means of value in these cases, and I always had and have a reasonable doubt as to their real efficacy in the hands of others.

As to the later surgical methods of Krause and Heryng by means of punching and curetting—these I must admit rarely make an appeal to me, especially the former. To punch out a bit of infiltrated, somewhat hardened, or œdematous tissue, over the intact arytenoid cartilage, I do not regard as indicated or desirable. Even incisions or punctures of these swellings are only profitable when the tissues are soft relatively and permit serous fluid to exude in appreciable quantity, as would be the case, of course, in soft œdema of the larynx and when notable stenosis with stridor was thus occasioned. Then, of course, with a properly shielded or curved lancet or knife, very great temporary relief from a very severe and sometimes imminently dangerous condition may be afforded.

If the ulceration be localized, if it be single, or a few ulcerations at most, these may be occasionally curetted moderately with some advantage, and while I have not attempted it myself, I do not object. Such a localized ulcer is not infrequently found underneath—or rather below—the polypoid excrescence of the interarytenoid fold. After the excrescence has been in part or wholly removed by forceps, the ulcer itself may be curetted before a local application is made. It is usually advisable before curetting is done or, indeed, the stronger pigments are applied, that a local anesthetic of cocaine should be made by a swab or spray. This application need not be very strong; a 4 per cent. solution is often sufficient.

Formerly, when I found a patient suffering with laryngeal pain and distress from ulceration and subsequent infiltration or perichondritis, I applied morphine, iodoform, or both combined, frequently to the parts, and thus lessened for a short time the patient's suffering and rendered deglutition somewhat easier in a few instances.

Again, position, notably that of Wolfenden, in which the patient's head hangs over the bed and fluid is sucked through a rubber tube from a mug or pitcher below, will afford relief to swallowing. Today we obtain more relief of pain probably in all abraded surfaces from the frequent local use of orthoform than by

any other known agent. Fortunately, too, orthoform is innocuous, and on this account may be used frequently and by the patient himself whenever required. Leduke's bent hard rubber tube, which may be inserted well back in the throat and through which the orthoform, placed in the orifice of the other extremity, may be aspirated strongly, offers a ready means to the patient to accomplish his purpose. From the experience and reports of many competent observers during latter years no application to ulcers of the larynx has received stronger endorsement than that of lactic acid. Applied in 10 to 80 per cent. solution, or even pure, it modifies the ulceration very favorably. Indeed, it not rarely seems to help the complete healing of the ulcer when single and localized. A local anesthetic is often required before and after its application, and especially is this true whenever curetting has been practised prior to the application of the lactic acid. If the lactic acid is applied locally in strong solution or pure, it should be done with care, so as to avoid undue pain and distress. If used on a swab or brush, any excess of acid should be gotten rid of before it is applied, because if a drop should fall into the larynx, notable spasm of the larynx, sometimes very threatening, will immediately follow.

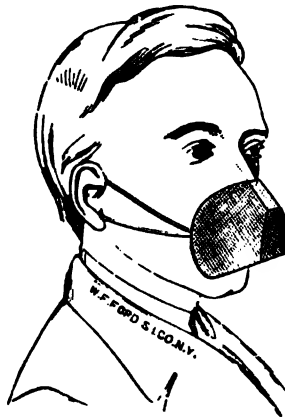
While I am willing to admit the utility of lactic acid, it is now pretty well shown by the report of H. G. Felkin<sup>6</sup> that its curative effects are markedly increased by complete rest to the larynx, as is afforded by insistence upon prolonged, absolute silence. Felkin's report embraces several cases which belong to him, and some also to Sir Felix Simon mutually. In those instances of numerous small ulcers outside the larynx known as upper tuberculous laryngitis, and in which the prognosis is specially bad, I disapprove of the use entirely of curetting, applications of lactic acid, etc. They cause considerable distress, are of no possible use, and are not justified at all when we consider the advanced, or very threatening condition of the patient from the point of view of the local pulmonary changes, or the general tuberculous infection, which almost invariably accompanies them.

In a few rare cases in which the epiglottis is the seat of deep ulceration, accompanied by very painful dysphagia, it has been found advisable to excise it either by means of a suitable knife or by the galvano-cautery snare. Notable relief from pain has followed in more than one instance, but the result at best has only been temporary, for in a brief period of time the patient has died because of the rapid inroads of disease already far advanced and very infectious in type. Seldom, either from this operation, or curetting, or punching, has any considerable or annoying hemorrhage occurred. One exception should be made in the case of operation

<sup>6</sup> Brit. Med. Jour., 1907, i, 1421.

on the swollen ventricular bands. Here, indeed, notable and worrying hemorrhage has occurred after deep curetting.

I now come, finally, to what I regard as by far the most important local measure to be employed by every sufferer from laryngeal tuberculosis at any stage of the disease, and that is the frequent, persistent, long-continued use of the perforated zinc inhaler (see figure) with inhalations of creosote and alcohol, or, when there is much irritative cough, of beechwood creasote, alcohol, and spirit of chloroform in equal parts. This is no new fact to me, but has become more and more a firm conviction. I have already several times directed attention to it, and I now reiterate it because of its great value. In 1885, at the second meeting of the Climatological Association, I read a paper on antiseptic inhalations, in which I first directed attention to the great value of these inhalations in many forms of laryngeal,



Perforated zinc inhaler.

bronchial, and even pulmonary disease. Later, in my little work on *Inhalers and Inhalants*, I again affirmed the value of these inhalations. And in more than one article in medical journals, or in remarks before societies, since that time, I have recurred to their importance. These inhalations modify sputum favorably, diminish its quantity, lessen cough, thus promoting rest, sleep, and nutrition, and general improvement physically, and in some instances appear to be the means through which the patient has gotten rid of tubercle bacilli permanently. I know of absolutely no other method, no other local application, no surgical measure, which will afford anything like the same amount of relief to symptoms and hasten and promote cure in suitable cases to the same degree as will the perforated zinc inhaler with the inhaling fluid recommended.

It is unnecessary for me at this time to give all my reasons why the skepticism made known and objections urged against the systematic

and continued use of the perforated zinc inhaler fail completely to establish the value of the objector's or doubter's position. The arguments and statements that I have given previously in favor of the use of the zinc inhaler, with the records of many cases observed by me, may be found in the papers and book referred to. Dr. Austin Flint, Sr., further pointed out its great utility in a series of cases of pulmonary phthisis observed by him and published many years ago. This fact I have already referred to.<sup>6</sup>

Only within a brief period, Dr. Lees, late physician to St. Mary's Hospital, London, England, stated, in his farewell address at that institution, that "during the past two or three years he had treated all his cases of this disease (pulmonary tuberculosis) with continuous inhalations by means of a Yeo's respirator,<sup>7</sup> on which was placed a mixture of carbolic acid, creosote, iodine, alcohol, ether, and chloroform. The inhaler<sup>8</sup> is worn day and night, and removed only at meal times. Six or eight drops of the mixture are dropped on the sponge of the inhaler every hour while the patient is awake, and several times during the night. This rapidly relieves cough, and *patients seem to derive great benefit from its use.*" It is a great help and encouragement to me to find unqualified support of what I have believed for so long a time from such a distinguished and accurate observer who has written truly, well, and with wisdom about several other most important matters relating to practical medicine—notably, the great value of blood letting in pneumonia, and the utility of the salicylates and sodium bicarbonate, combined and in large doses, in the treatment of acute articular rheumatism.

"Dr. Lees closed his address with a comparison of the good results which medical treatment can obtain in acute bacterial invasions with the disappointing failure of the most modern methods of therapeutic inoculation in these diseases—a necessary encouragement in these days of pessimism and skepticism as to the value of the drugs and methods which we have used so long."

Last winter I had a patient under my care at the clinic of the Bellevue and University Hospital Medical College, who had advanced pulmonary tuberculosis. His cough was most distressing and his nights, in consequence, sleepless. Nothing gave him any relief except the use of the perforated zinc inhaler. A case of bronchitis, with distressing cough and dyspnoea, reported by me,<sup>9</sup> was only relieved by means of the inhaler. A patient of mine suffering from pulmonary tuberculosis at the stage of infiltration with numerous bacilli in the sputum, one year ago, has been more helped, in my judgment, by the continued use of the zinc inhaler than in any other way, or by any other single measure. I consider this patient now almost

<sup>6</sup> New York Med. Record, 1906.

<sup>7</sup> Yeo's respirator is almost precisely similar to the perforated zinc inhaler I make use of.

<sup>8</sup> New York Med. Jour., December 8, 1888, p. 617.

<sup>9</sup> Ibid., December 8, 1906, p. 900.

well, and at times no tubercle bacilli can be found. It is my conviction that, despite healthful surroundings, proper nourishment, correct habits, and suitable internal medication, his condition would be at present nothing like so good if he had not used the inhaler. Indeed, when he had neglected or given up its use for a time, he was not so well and the bacilli recurred.

I saw a patient last winter with general tubercular infiltration of both lungs, which probably involved a great portion of them. This man had one of the most distressing, continuous, unremitting coughs I have ever known. Almost every rational measure was tried in vain, by myself and others, to give him relief. After the use of the inhaler for many weeks he was like a new man, returned to his work, and his cough had almost, if not entirely, disappeared.

I cannot emphasize too strongly, in this connection, certain facts well known to those of us who have had long and watchful experience, and these are:

1. There is a certain proportion of patients affected with laryngeal tuberculosis, just as those with pulmonary tuberculosis, who do not recover, in whom the disease is not even arrested no matter what treatment may be followed. These cases remain stationary, perhaps, for a little while, but even this is doubtful, and, as a rule, despite all our efforts and doings, the disease marches steadily onward and gradually grows worse, until the final end comes.

2. While we cannot predicate absolutely, from the intralaryngeal evidences of tuberculous disease, as to the extent and stage of the tuberculous disease of the lungs, yet usually, if one localization of tuberculous disease is of bad augury, so is the other in the larger proportion of cases.

Of course, there are exceptions, but they are few, and sooner or later the rule will obtain in the greater number of instances and my statement be verified. This fact is important when we consider fairly what should be done in the individual case of laryngeal tuberculosis. Should we employ methods which are expensive, tiresome, distressing, and useless when we know perfectly well, or could if we only would, what the outcome is to be, or should we content ourselves with promoting our patients' comfort as best we can and effect as much euthanasia as possible in a disease which occasionally is one of the most distressing and heart-sickening that afflicts humanity?

Recently my attention has been directed to valuable researches made by W. Jobson Horne, of London. The results of these researches "show that 97 per cent. of the cases of phthisis experienced symptoms referable to the larynx at one time or another in the course of the disease and the investigation further went to show that the routine examination of the larynx, in persons suffering from symptoms suggestive of early pulmonary disease, would enable a diagnosis of phthisis to be made at a time when the stethoscope



yields no evidence, and that is at a time when the physician can be of greater service to the patient."

In 1905, Mr. Harold Barwell,<sup>10</sup> of London, read a paper on "The Choice of the Method of Treatment in Cases of Tuberculous Laryngitis, with a Plea for the Routine Inspection of the Throats of Consumptive Patients," the conclusion of which is entirely in accord with the feelings of Dr. Geo. L. Richards, of Fall River, Mass., and with my own, in regard to the subject. Barwell, quoted by Richards, writes: "Because it (tuberculous laryngitis) is common in all stages of phthisis, because it may cause no symptoms to attract attention, and because the early stages are much more amenable to treatment, and also because it produces one of the most painful and distressing forms of death, I most strongly urge that all cases of consumption should have their larynges inspected at regular intervals and as a matter of routine."<sup>11</sup>

Of course, in obscure cases, despite very careful laryngeal and physical examination, we should not ignore "one other valuable aid to the early diagnosis" of pulmonary and laryngeal tuberculosis, viz., "the use of tuberculin." It will frequently enable us, as Dr. Edward O. Otis writes, "to establish beyond a doubt the existence of the disease."<sup>12</sup>

We should also admit that occasionally we may be able by means of the Röntgen rays to recognize a pulmonary tuberculous process in an earlier stage than is possible by auscultation, or percussion.<sup>13</sup> Further, the discovery of tubercle bacilli in the feces<sup>14</sup> in obscure cases will alone sometimes make the diagnosis possible. "The application of tuberculin to the eye in diagnosis, which has been recently introduced by Prof. Calmette,<sup>15</sup> of Lille, France, gives promise of great advantages over the fever test."<sup>16</sup>

I should like to commend to everyone a very wise and thoughtful article<sup>17</sup> entitled "Exile and Drugs in the Treatment of Tuberculosis," by Dr. A. Jacobi, of New York. Nestor of our profession, he is also one of our wisest counsellors and most sincere of professional friends in the cause of intelligent, broad-minded, and thoroughly sane medical practice—in my humble judgment. "Modern medical science and art," he writes, "which have succeeded in appreciating the teaching that the best object of man's endeavor is man himself, have tried to utilize nature in all her bounties." Let us remember it always, I pray, and, besides, these other words of great import, "Life is short, and art long, occasion fleeting, experiment fallacious, and judgment difficult."

<sup>10</sup> British Med. Jour., 1905.

<sup>11</sup> Boston Med. and Surg. Jour., August 9, 1906.

<sup>12</sup> Ibid., September 12, 1907.

<sup>13</sup> Ibid., September 26, 1907, p. 420.—Percy Brown.

<sup>14</sup> New York Med. Jour., August 31, 1907.—M. Solis Cohen.

<sup>15</sup> Calmette's earlier observations are further confirmed by those of Dr. Wolff Eisner and other authorities at a meeting of the Berlin Medical Association, Lancet, December 28, 1907.

<sup>16</sup> E. R. Baldwin, "The Ophthalmo-Tuberculin Diagnostic Test: Some Clinical Observations," New York State Journal of Medicine, October, 1907, p. 413.

<sup>17</sup> Amer. Med., December 23, 1905, p. 1063.

I would add a few final words. I am familiar with the report and discussion before the Section on Medicine of the Academy,<sup>18</sup> in regard to the value of Kuhn's lung suction mask for the hyperemic treatment (Bier) of pulmonary tuberculosis. Neither report nor discussion has convinced me that this mask would prove so useful as the much cheaper, simpler, already widely and long time known perforated zinc inhaler, which I vaunt again with additional enthusiasm and conviction. What Dr. Willy Meyer states in his paper, apropos of Kuhn's mask, I reëcho emphatically for the perforated zinc inhaler.

"It will prove to be of especial value in dispensary practice and in the treatment of such phthisical patients as are not endowed with the riches of this world and cannot afford to leave their homes and their families. I, therefore, believe that the perforated zinc inhaler for the treatment of phthisical patients should be promptly introduced into sanatoria as well as in private practice, thus allowing patients afflicted with pulmonary tuberculosis to benefit from the perforated zinc inhaler."<sup>19</sup>

Eli H. Long<sup>20</sup> adds further testimony to the value of antiseptic inhalations in the treatment of laryngeal and pulmonary tuberculosis. "In pulmonary tuberculosis medicinal treatment has been in recent years greatly discounted, in comparison with out-of-door living, good nourishment, and proper adjustment of bodily rest and activity. But local treatment by the use of antiseptic inhalations, is so rational and so useful in incipient cases, as to easily take first place in the medicinal part of the treatment; and the less perfectly the hygienic treatment can be applied in any given case the more important becomes the inhalation treatment, though secondary in value."

At a recent meeting of the Practitioners' Society of New York,<sup>21</sup> I presented a patient who had been under my care for pulmonary tuberculosis. His disease is now arrested, if not cured. The result is due, as I believe, in addition to proper hygienic measures and a sojourn during the past winter at Asheville, N. C., to the prolonged, faithful use of the perforated zinc inhaler.

In conclusion I would again insist upon two things as most essential in the treatment of laryngeal phthisis locally: 1. Rest to the larynx.<sup>22</sup> 2. Dry vaporized antiseptic inhalations. To me the latter are by far the more important, because if they be used even singly they will effect curative results which the former alone can never accomplish.

<sup>18</sup> New York Med. Record, January 9, 1907, pp. 757, 793, 794.

<sup>19</sup> Cited textually from Dr. Willy Meyer's article in Med. Record, except for the substitution of perforated zinc inhaler for Kuhn's mask.

<sup>20</sup> New York State Jour. Med., June, 1908, p. 325.

<sup>21</sup> Med. Record, May 30, 1908, p. 921.

<sup>22</sup> Bardwell and Adams report in Brit. Med. Jour., June 8, 1907, six cases of laryngeal tuberculosis all markedly benefited by vocal rest. In four cases of ulceration these healed entirely. In every case improvement in the larynx was accompanied by improvement of the general condition and the condition of the lungs. All patients benefited greatly with an average treatment of five months and over.

**PRIMARY TUBERCULOSIS OF THE MESENTERIC GLANDS.<sup>1</sup>**

REPORT OF INFECTIONS WITH BACILLI OF THE HUMAN TYPE.

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BEFORE reporting the cases that form the subject of this paper, it may be profitable and interesting to bring together all other instances in which tubercle bacilli have been found, cultivated, and differentiated in mesenteric glands, in order to see whether we are justified in drawing any general conclusions. I shall not consider the question of the frequency with which primary mesenteric tuberculosis is encountered. This is a subject concerning which inexplicable differences of opinion still exist, as is indicated by a comparison of the English statistics, which show a primary lesion of the intestine and its glands 290 times among 1560 autopsies on children, that is, in 18.6 per cent., whereas, among 369 cases of tuberculosis coming to autopsy in New York and its environs, only 5 were of intestinal origin, a little more than 1.3 per cent.<sup>2</sup> Leaving this question open, let us turn to those cases in which the type of infecting organism has been isolated and studied. On reviewing the literature I have been able to find 71 instances in which this procedure has been followed.

Eighteen cultures were studied by the British Tuberculosis Commission, 27 by the German Commission, and 26 by other investigators. A cursory review of these cases, best seen when they are arranged in tabular form (Table I) brings to light the fact that the majority are instances of infection with the bovine type of bacillus; in fact, 44 of the 71, or 62 per cent., are of this nature. These figures are not conclusive in deciding the question as to the relative importance of bovine and human infection in general, for they consider only one group of cases, and, as I have said elsewhere,<sup>3</sup> only a consideration of a large number of unselected cases of pulmonary, intestinal, glandular, bone, and other infections can finally throw light upon the relative incidence and importance of these two groups of tuberculosis. As yet we have no data based upon such a series of cases. Both commissions have selected too many instances of abdominal tuberculosis to make their results of value from this point of view. The significance of their investigations lies in other directions. However, the fact that 62 per cent. of intestinal or mesenteric gland tuberculosis proved to be of bovine origin is

<sup>1</sup> Read before the New York Pathological Society, February 19, 1908.<sup>2</sup> AMER. JOUR. MED. SCI., 1907.<sup>3</sup> Archives of Pediatrics, June, 1907.

worthy of note. It means that the tubercle bacillus of cattle is a factor that cannot be disregarded, as Koch maintains, in its pathogenicity to man. Again, when this 62 per cent. is compared to the percentage of bovine infection which has been demonstrated in other organs of the body, it emphasizes the fact that the mesenteric glands form the chief portal of entry for the bovine bacillus, with the tonsils alone to share this distinction.

TABLE I.—A SUMMARY OF REPORTED CASES OF PRIMARY MESENTERIC GLAND TUBERCULOSIS, WITH THE TYPE OF BACILLUS.

Source.	Human.		Bovine.	
	Children.	Adults.	Children.	Adults.
British Tuberculosis Commission . . . . .	8	..	10	
German Tuberculosis Commission * . . . . .	7	5	15	
Smith, Trans. Assoc. Amer. Phys. . . . .	1	..	1	
Smith, AMER. JOUR. MED. SCI., 1904 . . . . .	1	2		
Smith and Brown, Jour. Med. Research, September, 1907 . . . . .	..	1	1	
Ravenel, Univ. Penna. Med. Bull., 1902 . . . . .	..	..	1	
de Schweinitz, Dorset and Schroeder, Bureau of Animal Indust. Bull., 52, Pt. 2, 1905 . . . . .	..	..	2	
Fibiger and Jensen, † Berl. klin. Woch., 1902, 1904, 1907 . . . . .	1	1	5	
Damann and Mühlmeier, Untersuch. der Tb. der Menschen und Tiere, 1905 . . . . .	..	..	..	1
Hoelsinger, Inaug. Diss., Giessen, 1907 . . . . .	..	..	..	1
L. Rabinowits, Arbeit. a. d. Patholog. Inst., Berlin, 1906; Berl. klin. Woch., 1907 . . . . .	..	..	2	1
Westenhoefer, Berl. klin. Woch., 1903 . . . . .	..	..	1	
Eber, Beiträge z. klinik der Tuberkulose, 1905 . . . . .	..	..	2	
Fife and Ravenel, Proc. Phila. Pathol. Soc., 1905 . . . . .	..	..	1	
Total . . . . .	18	9	41	3

\* In one case, not included in the table, both types were isolated from the mesenteric glands. In two cases in the table a bacillus of different type was found elsewhere than in the mesenteric glands.

† Including cases 4, 5, 6, 7, 8, 11, 12 of authors.

The next point which compels notice is that, of these 71 cases, only 12 occurred in adults. The significance of these figures is somewhat dimmed by the fact that the glands of children were especially selected for the investigations. Nevertheless, although this may not be the correct ratio, all autopsy records show the marked preponderance of mesenteric gland tuberculosis in children as compared to adults. The statistics are absolutely sufficient, however, if we consider children and adults separately in two distinct groups and

compare the proportion of human and bovine infections in each. Such a comparison reveals that, of the 59 cases in children, 41 (69.5 per cent.) were bovine infections, some showing an atypical strain of bacillus, whereas, of the 12 adult cases, only 3 (25 per cent.) were of bovine origin. This difference in the type of infection cannot be due solely to increased exposure on the part of young children to food contaminated with bovine bacilli, such as infected milk, for adults in the course of many years must be similarly exposed. We must attribute this difference to a diminished natural resistance on the part of the child, in the nature of an increased permeability of the intestine, or to lack of protective power of the lymph nodes, or we must concede a degree of acquired immunity toward bovine bacilli on the part of the adult.

When we inquire into the course of the disease produced by the two types of bacilli in mesenteric gland tuberculosis, we find no points of differentiation. In either case the disease is generally progressive. However, instances of limited infections occur in each variety, and are encountered generally when the tuberculous lesion is of secondary importance, the cause of death being some other infectious disease. For example, the bovine type has been found in a solitary calcareous node,<sup>4</sup> and again in the ascitic fluid of a patient who recovered and was well three years later.<sup>5</sup>

As regards the character of the lesions, Baumgarten has claimed that the human type of bacillus more commonly caused caseation, whereas the bovine organism incited calcification. Viewed from this standpoint, the sixty-nine cases show no distinctions. Caseation was found in all but four instances, and these were of the human variety. Whether calcification develops probably depends more upon the virulence of the bacillus than upon its type, and also upon the peculiarities of its host. For instance, the second interim report of the British Commission shows that calcification was almost universally found in the mesenteric glands of swine, calves, and cows fed with human sputum, which may, I believe, be interpreted in this way. Finally, it should be mentioned that the German Commission reports that in seventeen cases of tuberculosis found at autopsy in children dying of acute infectious diseases, animal inoculation proved negative, in spite of the fact that tubercle bacilli were found in these nodes in eight instances, in some cases in exceptionally large numbers. This emphasizes the limitation of animal inoculation and the necessity of microscopic examination in the diagnosis of tuberculosis. It furthermore shows the resistance of children to tuberculous infection and their ability to arrest the disease by killing the invading bacilli.

<sup>4</sup> Berl. klin. Woch., 1907, Nr. 2.

<sup>5</sup> Untersuchungen über die Beziehungen zwischen der Tuberkulose der Menschen und der Tiere, Hanover, 1905.

The three cases that I report are instances of primary mesenteric gland tuberculosis:

CASE I.—A. C., a child, aged three years and nine months, was admitted to the New York Foundling Asylum for malnutrition. No history was obtained. The autopsy, performed January 23, 1907, by Dr. Howland, who kindly sent me the pathological material, disclosed the following unexpected anatomical conditions: Enlargement of the follicles in the lower portions of the small intestine, marked prominence of the Peyer's patches, with three or four deep transverse ulcerations; enlargement and caseation of the mesenteric glands; moderate enlargement of the spleen. The lungs were negative, the mediastinal glands slightly enlarged. The pathological diagnosis was tuberculosis of the intestine and mesenteric glands.

Smears made from the cheesy mesenteric glands showed a few tubercle bacilli. No bacilli were seen in smears from the small, slightly anthracotic bronchial glands. On January 25 two guinea-pigs were inoculated subcutaneously with bits of mesenteric gland, and one with bronchial gland tissue. Twenty-one days later the pigs inoculated with mesenteric gland were chloroformed, as they showed enlargement of the inguinal glands, although they had both gained slightly in weight. Both were found to be tuberculous. Tissue from the inguinal glands, iliac glands, and spleen were used for culture on dog serum and egg media. The pig inoculated with the bronchial gland was chloroformed after thirty-four days and showed no tuberculosis. Cultures were readily obtained from the spleen and inguinal glands; they grew after twenty-three days on the serum and later on the egg media. They appeared as round colonies at the upper part of the tube where the media was in an extremely thin layer. Later they spread out in heavy membranes. The bacilli were in the form of straight rods from 1.5 to 2  $\mu$  in length, and were similar in all the tubes. In subsequent cultures they varied considerably in length and contour. Thus, in facility of culture and in morphology they resembled the human type. Intravenous inoculations into rabbits confirmed this opinion. For this purpose 0.5 c.c. of a suspension of bacilli in salt solution, corresponding in density to a twenty-four-hour bouillon culture of typhoid bacilli, was employed. As the table (Table II) shows, the bacilli possessed but slight virulence toward rabbits, causing only local lesions after a period of two and three months. Bovine bacill when thus inoculated invariably produce a generalized tuberculosis.

CASE II.—P. H., an infant, aged twenty-two months, was admitted to the Babies' Hospital, to the service of Dr. Holt, to whom I am indebted for the following information: The family history showed that the father had suffered from a cough for an indefinite period. The child was nursed for four months and then fed on raw milk mixtures. It had a previous history of pertussis and measles, and had been in the hospital twice before, once suffering from an

TABLE II.—DATA OF INOCULATION OF RABBITS WITH PURE CULTURES OF TUBERCLE BACILLI.

	Total age of culture.	Number of transfer.	Age of culture.	Amount inoc- ulated.	Number of rabbit.	Date and method of inoculation.	Result.	Remarks.
Foundling Asylum . . .	44 days	Second	11 days	0.5 c.c.	250	Ear vein, March 31, 1907	Chloroform, June 9 (2 months, 9 days)	A few foci in kidneys and an- terior part of lungs.
	44 days	Second	11 days	0.5 c.c.	217	Ear vein, March 31, 1907	Chloroform, July months, 6 days)	Foci in kidneys.
Babies' Hospital . . .	37 days	Second	10 days	0.5 c.c.	213	Ear vein, January 1, 1907	Chloroform, February 6 (2 months, 20 days)	Extensive tuberculosis of lungs.
	37 days	Second	10 days	0.5 c.c.	207	Ear vein, January 1, 1907	Chloroform, February 17 (3 months)	A few foci in lungs and kidneys.
Bellevue Hospital. . . .	53 days	Third	12 days	0.5 c.c.	299	Ear vein, January 16, 1907	Chloroform, April 18 (3 months, 2 days)	Tuberculosis of iris. Foci in kid- neys and lungs.
	27 days	First	27 days	0.5 c.c.	208	Ear vein, June 5, 1907	Chloroform, August 5 (2 months)	Two foci in lungs; a few in kid- neys.
	27 days	First	27 days	0.5 c.c.	209	Ear vein, June 5, 1907	Chloroform, August 5 (2 months)	Large foci and kidneys.

"acute gastrointestinal toxemia," the second time from "bronchitis and anemia." It was now admitted on account of diarrhoea.

Examination showed the baby prostrated, abdomen lax, and glands not palpable, except those in the inguinal region, which were the size of shot. The temperature on admission was 104.3° F.; the weight, 21 pounds 10 ounces. A diagnosis of tuberculous enteritis was made. Delirium soon supervened and was followed by death.

The autopsy, performed on September 3, 1906, by Dr. Martha Wollstein, whom I have to thank for the pathological material, revealed the following conditions: Tuberculosis of the intestines and mesenteric lymph nodes, fatty liver, splenic tumor. Lungs and bronchial lymph nodes negative. Cultures of the heart's blood showed no growth. Sections of the spleen, liver, lung, ileum, and mesenteric lymph nodes were made. On microscopic examination the liver, lung, and intestine showed no tuberculosis. In the spleen there were many young tubercles. The mesenteric glands showed numerous giant cells with peripherally arranged nuclei, as well as large areas of caseation.

From this autopsy a piece of liver, which appeared normal, bronchial glands of a deep-red color and slightly enlarged, but otherwise negative, and a few large cheesy mesenteric glands were sent to me. Bacilli, many of them long and of beaded appearance, were found on the smears from the mesenteric glands. Five guinea-pigs were at once inoculated subcutaneously, one with liver tissue, and two with bronchial and mesenteric gland tissue respectively. Of the five, the only one to develop tuberculosis was one of those inoculated with mesenteric gland. The autopsy of this pig showed nothing requiring mention excepting marked enlargement of the retrosternal lymph node. This lesion was found in other pigs often when there was but little tuberculous involvement of the lungs or surrounding tissues.

Cultures were made as in the previous case, but owing to a mishap no growth resulted, so that new cultures were made from a pig which had been inoculated on November 8 with some incubated tissue. In twenty-one days discrete colonies appeared upon one egg tube and one dog-serum tube, and soon became confluent and heavy. The individual bacilli were slightly curved and varied in length from 1.5 to 2.5. Virulence tests made with the second and third generation of bacilli, as shown by the table, proved this strain to be of virulence similar to that isolated in Case I. The reaction test on glycerin bouillon confirmed the conclusion that we were dealing with a bacillus of the human type. When inoculated, the bouillon was 2.1 per cent. acid to phenolphthalein, and eighty-two days later it was found to be 2 per cent. acid. According to this culture test, devised by Theobald Smith,<sup>6</sup> bovine bacilli when grown upon acid

<sup>6</sup> Jour. Med. Research, vol. xiii, No. 3.



glycerin bouillon tend to bring the media toward the alkaline reaction, whereas in human cultures the reaction curve, although at first "moving toward the neutral point, soon swings back to a greater acidity."

The father of this child is now strong and healthy, and does not cough. As the infant had been fed on raw milk, we might have been inclined, judging from the history alone, to consider this a case of bovine infection.

CASE III.—This material was obtained from the autopsy of W. M., a boy, aged seventeen years, admitted to the service of Dr. Gilman Thompson, at Bellevue Hospital. His family and previous history gave no indication of tuberculosis. At the time of admission to the hospital, he complained of abdominal pain and diarrhoea of three months standing, accompanied by marked loss of weight and strength.

Examination showed the boy's general condition to be poor. A few rales were heard in the lungs. The abdomen was held rigid and was generally tender; percussion elicited dullness in the flanks, changing with change of position. The diagnosis was chronic pulmonary tuberculosis, tuberculous peritonitis, and tuberculous enteritis. Death followed four days after admission.

The autopsy, performed three hours after death by Dr. Norris, who kindly furnished me the material for examination, disclosed the following pathological conditions: Primary acute tuberculous hyperplastic enteritis, acute suppurative peritonitis, intestinal flora on smears; perforation of ileum; acute serofibrinous pleuritis; acute parenchymatous nephritis and hepatitis; suppurative sphenoiditis and otitis media; persistent thymus; bronchial lymph nodes slightly anthracotic, otherwise negative; mesenteric nodes enormously enlarged, most of them hyperemic, the largest showing on section yellowish areas of necrosis.

The large mesenteric glands which were sent to me on April 15, 1907, were not typically tuberculous on macroscopic examination, resembling somewhat sarcomatous glands. A long search revealed a few acid-fast bacilli. Microscopic examination showed caseation in some sections, in others only a marked swelling and proliferation of the endothelial cells lining the perifollicular spaces. As in the other cases, passage through guinea-pigs was used to obtain pure cultures, bits of glandular tissue being inserted into subcutaneous pockets in the abdominal wall. In this instance both animals died after five days, so that the inoculation of two pigs was repeated with tissue thoroughly washed in salt solution. Both pigs gained in weight, but showed marked enlargement of the inguinal glands. They were chloroformed on May 5, 1907, twenty-three days after inoculation. Cultures were obtained from the inguinal and iliac glands. The growths were profuse and glistening and were successfully transferred to glycerin bouillon. The bacilli resembled

those isolated in Case I, and were mainly straight rods 1.5 to 2.0  $\mu$  in length, a few being longer. A suspension inoculated into the ear veins of two rabbits proved this strain to have a low virulence.

**SUMMARY.** A review of cases of primary mesenteric gland tuberculosis in which the type of bacillus has been differentiated shows that over 60 per cent. have been caused by the bovine type of bacillus. Among children the bovine infections greatly prevailed, whereas in adults infections with the human variety were in the majority. No pathological or clinical differentiation of the two forms of tuberculosis is as yet possible. In children, as well as in adults, bovine or human tuberculosis may become limited and healed and the bacilli may die. In striking contrast to the cases summarized above, it is interesting to note that those reported in this paper, two in children and one in a young adult, were due to the human variety of bacillus, as shown by the morphology, cultural characteristics, and virulence of the isolated strains.

## BLOOD CULTURES IN TYPHOID FEVER.<sup>1</sup>

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THE principles established by Castellani and Schottmüller concerning the bacteriology of the blood in typhoid fever and the knowledge that we have in positive blood cultures a means of determining early and with certainty the presence of this disease, have induced many investigators to search for methods of facilitating the work. The recent advances have, therefore, been mainly in the line of demonstrating the ease with which the work may be done; but as the literature indicates, the frequency of positive findings is not greater with the new than with some of the old methods.

Much of the difficulty hitherto experienced in cultivating the bacilli has been attributed to the bactericidal power of the blood. To overcome this hindrance Castellani<sup>2</sup> used large quantities of bouillon, and obtained positive results in 78 per cent. of the cases. Schottmüller,<sup>3</sup> however, used agar, the blood being present in the proportion of 1 to 3 of the medium. He was successful in finding the bacillus in 81 per cent. of the cases.<sup>4</sup> Numerous other methods

<sup>1</sup> Preliminary studies were presented before the New York Pathological Society, in October, 1906.

<sup>2</sup> *Settimana Medica*, 1899.

<sup>3</sup> *Münch. med. Woch.*, 1902, Nr. 38.

<sup>4</sup> If we were to adhere to the theory that the blood of a typhoid fever patient exerts marked inhibitory influence upon the development of the typhoid bacillus, Schottmüller's success in the work must be explained on the hypothesis of Eppenstein and Korte, that agar in solidifying destroys or diminishes the bactericidal properties of the blood.

have been employed for cultivating the bacillus. Lemiere<sup>5</sup> was successful with cultures made from defibrinated blood. Eppenstein and Korte<sup>6</sup> grew the bacilli in oxalated blood. Müller and Graef<sup>7</sup> observed the growth of the bacilli in the fibrin net-work of clotted blood. Klodnitzky<sup>8</sup> succeeded in growing the bacilli from blood laked in ordinary sterile water. In twenty-five cultures made in our laboratory, we found multiplication of the bacilli in oxalated blood twenty-three times (without the addition of any nutrient material).

From these data it will at once be seen that the unfavorable influence of the blood upon the growth of the bacilli has been considerably overrated. We cannot escape from the fact that with a variety of methods the results obtained by nearly all investigators have been uniform. It seems that in working with one or another method many of the real conditions underlying the success or the failure of the work have been overlooked.

Thanks to the coöperation of the attending staff of the Mt. Sinai Hospital, I am able to report 158 blood cultures taken in 131 cases of typhoid fever at different stages of the disease (this series includes 2 cases of paratyphoid, 1 of mixed infection with a streptococcus, and 1 case in which secondary infection by the pneumococcus occurred). The subject matter will be taken up in the following order: (1) A description of the technique of obtaining the blood and of the media used. (2) The results; a comparison of the advantages of the various media; a note on the characteristic appearance of the colony of the typhoid bacillus in glucose agar; and a note on 2 cases of mixed infection. (3) The results in relapses. (4) The relationship of the positive findings to the presence of the Widal reaction. (5) The relation of the bacteremia to the stage, course, and severity of the disease. (6) The significance of negative cultures. (7) A note on the possible significance of the bacteremia in relation to the prognosis. (8) Conclusions.

**TECHNIQUE.** The method used in obtaining the blood is that introduced into the laboratory by Dr. Libman.<sup>9</sup> The blood is usually withdrawn from one of the veins in the bend of the elbow. In stout patients and in children, in whom these veins are often invisible or too small, a vein on the back of the hand or the dorsum of the foot has occasionally been used. It is wise to inspect these different parts first, and see where one can best find a vein of sufficient size. After the constriction bandage has been applied above the part selected and the field has been scrubbed with soap and water, it is rubbed with ether, alcohol, and finally with 1 to 500 solution

<sup>5</sup> Münch. med. Woch., 1906, Nr. 32.

<sup>6</sup> Ibid., Nr. 24.

<sup>7</sup> Centralbl. f. Bakt., 1907, vol. xliii, Heft 8.

<sup>8</sup> Russki Vrach, vol. vi, Nos. 27, 28, and 29.

<sup>9</sup> Johns Hopkins Hosp. Bull., July, 1906.

of mercuric bichloride. Because a large number of media was used for each blood culture, it was necessary to withdraw a moderately large quantity of blood, 10 c.c. or more. It will be shown later that although the use of so large an amount of blood increases the chances of obtaining a positive result, a smaller amount is usually sufficient. When the work was first taken up bouillon media were mainly used; later the series of eight media used as routine in the laboratory were employed. In the course of most of the recent work the following eleven media were employed:

1. Plain nutrient bouillon (from meat infusion, 0.9 per cent. acid to phenolphthalein<sup>10</sup>) in flasks containing 120 c.c.
2. 2 per cent. glucose bouillon (titre and quantity like medium 1).
3. Plain nutrient agar (0.9 per cent. acid to phenolphthalein).
4. Plain nutrient agar to which  $\frac{1}{4}$  to  $\frac{1}{2}$  volume of ascitic serum has been added.
5. 2 per cent. glucose agar (titre same as that of the plain agar).
6. 2 per cent. glucose agar with  $\frac{1}{4}$  to  $\frac{1}{2}$  volume of ascitic serum.
7. Plain agar (neutral in reaction to phenolphthalein).
8. 5 per cent. glycerin agar (0.9 per cent. acid).
9. 10 c.c. of Conradi's bile medium.
10. 5 c.c. of Kayser's bile medium.
11. 10 c.c. of a 0.2 per cent. solution of ammonium oxalate.

The work was more or less developmental in character, and was carried on without any preconceived notions concerning the possible merits of one or another medium. The eight media referred to above, as belonging to our routine series, were numbers 1 to 8 of the above list. The latest studies were made with media 1, 2, 5, 9, 10, and 11. The oxalated solution was used for two reasons: first to test the growth of bacilli in oxalated blood without the addition of any nutrient material, and second, to test the efficiency of this solution as an intermediate measure in blood culture work between the bedside and the laboratory.<sup>11</sup> In the use of the bile media, the directions given by Conradi<sup>12</sup> and Kayser<sup>13</sup> were closely followed. In each series after the blood was withdrawn it was rapidly distributed into the media and incubated at 37.5° C. The cultures were observed from three to seven days, and careful records were made both as to the time of appearance and the features of the growths. The following summaries give the results obtained with the different media:

<sup>10</sup> The titre of 0.9 per cent. acid was chosen because it was found to give a better growth of typhoid bacilli than more acid media. It is part of our routine to make frequent sub-inoculations from each of the fluid media upon glucose serum agar and plain nutrient agar as well as plain nutrient bouillon and glucose bouillon.

<sup>11</sup> Epstein, AMER. JOUR. MED. SCI., September, 1907.

<sup>12</sup> Münch. med. Woch., 1906, Nr. 34.

<sup>13</sup> Ibid., Nr. 17.

## SUMMARY I.

Medium.	No. of cultures.	Amount of blood, C.c.	Positive results.	Negative results.	Positive results in per- centage.	Time in hours.
1. Plain bouillon . . . . .	81	2	61	20	75	48
2. 2 per cent. glucose bouillon . . . . .	86	2	70	16	81.4	38
3. Plain agar . . . . .	31	2	12	19	38.7	50
4. Plain agar and serum . . . . .	26	1.5	8	18	31	68
5. 2 per cent. glucose agar . . . . .	83	2	67	16	80	31
6. 2 per cent. glucose agar and serum . . . . .	20	1.5	8	12	40	58
7. Neutral plain agar . . . . .	16	1.5	1	15	6.6	
8. 5 per cent. glycerin agar . . . . .	32	2	12	20	37.5	68
9. Conradi (10 c.c.) . . . . .	28	1.5	16	12	57.5	26
10. Kayser (5 c.c.) . . . . .	29	2	17	12	58.6	31
11. Ammonium oxalate solution (10 c.c.) . . . . .	25	3.5	23	2	92	29

## SUMMARY II. THE TWO BOUILLONS COMPARED.

Both bouillons were used simultaneously in 80 positive cultures.

Both bouillons were positive in 51 cultures, 63.7 per cent.

Both bouillons were negative in 8 cultures, 10 per cent.

Plain bouillon was positive

2 per cent. glucose bouillon was negative } in 7 cultures, 8.7 per cent.

Plain bouillon was negative

2 per cent. glucose bouillon was positive } in 14 cultures, 17.4 per cent.

So that in all, plain bouillon was positive in 58 of the 80 cultures, 72.5 per cent., and

2 per cent. glucose bouillon was positive in 65 of the cultures, 81.25 per cent.

Total positive results for both bouillons, 90 per cent.

The average total amount of blood used for the bouillon media was 4 c.c. per culture.

## SUMMARY III. AGAR MEDIA COMPARED.

A. Plain agar

2 per cent. glucose agar } used together in 26 cultures.

Both were positive in 10 cultures, 38.4 per cent.

Both were negative in 3 cultures, 11.5 per cent.

Glucose agar was positive alone in 13 cultures, 50 per cent.

Plain agar was positive alone in 0 cultures, 0 per cent.

B. 5 per cent. glycerin agar

2 per cent. glucose agar } used together in 31 cultures.

Both were positive in 10 cultures, 30.1 per cent.

Glycerin agar was positive

Glucose agar was negative } in 2 cultures, 6.2 per cent.

Glycerin agar was negative

Glucose agar was positive } in 14 cultures, 45.1 per cent.

Of the total 31 cultures, 2 per cent. glucose agar was positive in 24 cultures, 77.4 per cent.;

whereas glycerin agar was positive in 12 cultures, 38.4 per cent.

## SUMMARY IV. BILE MEDIA COMPARED.

Both media were used in 27 cultures.

Both media were positive in 11 cultures, 41.8 per cent.

Both media were negative in 6 cultures, 22.2 per cent.

Conradi medium was positive

Kayser medium was negative } in 4 cultures, 14.8 per cent.

Kayser medium was positive

Conradi medium was negative } in 6 cultures, 22.2 per cent.

In the 27 cultures in which both bile media were used, the total positive results obtained were 21 cultures, 77.8 per cent.

The average total amount of blood used for the bile media was 3.5 c.c. per culture.

## SUMMARY V. AMMONIUM OXALATE SOLUTION COMPARED WITH THE OTHER MEDIA.

Used in 25 cultures, positive in 23.

- A. Ammonium oxalate solution } used together in 19 cultures.  
Plain bouillon

Growth appeared in the oxalate blood in 17 cultures, and in plain bouillon in 13 cultures

- B. Ammonium oxalate solution } used together in 20 cultures.  
2 per cent. glucose bouillon

Growth in oxalate blood in 18 cultures.

Growth in glucose bouillon in 17 cultures.

- C. Ammonium oxalate solution } used together in 23 cultures.  
2 per cent. glucose agar

Growth in oxalated blood in 21 cultures.

Growth in glucose agar in 20 cultures.

- D. Ammonium oxalate solution } used together in 13 cultures.  
Conradi medium  
Kayser medium

Growth in oxalated blood in 11 cultures.

Growth in Conradi's medium in 8 cultures.

Growth in Kayser's medium in 7 cultures.

Average amount of blood used in this medium was 3.5 c.c.

In studying these results we can readily see which media appear to be best suited for the work. We find that the media can be arranged in two groups, one of which is distinctly favorable to the growth of the bacilli and another which is unfavorable. It is evident, of course, that the word "unfavorable" must be used cautiously, because in any one blood culture the organisms may be few in number and, therefore, may appear on some of the media and not on others. In such instances it is greatly a matter of chance which medium gives positive results. The bacterial invasion of the blood in typhoid fever appears to be more uneven than it is in infections by other bacteria, for even in some cases in which the bacteria are comparatively numerous, we find that the given amount of blood divided equally into like portions of the same medium gives an unequal number of colonies in each portion. This difference is at times very striking. Müller and Graef, in their cultures from clotted blood, had the same experience. I am not able to say what the cause of the uneven distribution is; possibly clumping of the organisms plays some part. I have at times found that fully developed colonies of typhoid bacilli (of the type to be later described) would appear on 2 per cent. glucose agar within the first sixteen hours of incubation, and then thirty-six to forty-eight hours might elapse before any more colonies appeared on the same plate. We must assume from this fact that, as a result of a conglomeration or actual clumping, the respective colonies arise from different numbers of bacilli.

In this connection it may be stated that in the entire series of 158 cultures I have at no time seen so large a number of bacteria in the blood as that observed by Schottmüller and by Schueffner.<sup>14</sup> Whether this difference is due to difference in the type of the cases

<sup>14</sup> Münch. med. Woch., 1907, Nr. 35.

studied or not, I cannot determine; possibly differences in technique may account for the discrepancy.

From the study of the variations which occur in the number and growth on the different media and different portions of the same medium, I am inclined to the belief that up to a certain degree the media exert but little influence on the result of the culture. The bacilli will grow on any medium provided such a medium is not actually antagonistic. It appears that bacilli fail to grow well in neutral media and in media the titre of which is above 0.9 per cent. acid. The experiments of Müller and Graef with clotted blood as well as those of Eppenstein and Korte with oxalated blood, and those of Meyerstein<sup>15</sup> with bile salts led to the belief that the fluidity of the blood was essential to the development of the bacilli. The later work of Müller and Graef showed that the fluid state of the blood for growth is not necessary, as they had observed the growth in the fibrin net-work of clotted blood.

It is likely that a number of bacilli which reach a culture medium are impaired in their vitality in consequence of the detrimental influence to which they are exposed in the body; so that the blood withdrawn for the culture may contain bacilli, few of which, if any, are viable. But the claim so frequently made that the failure of the bacteria to grow is wholly due to the continuation of the bactericidal action of the blood (*in vitro*) is not supported by experience. The work of Eppenstein and Korte bears evidence to the contrary. They conclude from their experiments that the bacillus develops an immunity against the bactericidal action of the blood of the host. This view gains support from the fact that the bacteria multiply in defibrinated, oxalated, laked, and clotted blood without the addition of any nutrient medium.

What has been said of the cultures on ordinary media applies also to the bile media of Conradi and Kayser. The results with these methods show no advantages over the ordinary methods. My own results indicate a distinct disadvantage. I found no evidence that bile uniformly augments the growth of the bacilli. The experiments which Meyerstein recently performed proved that the bile salts do not possess any "anreicherung" influence upon the growth of the typhoid bacilli. His observations, as well as those of Nicolle and Adil-Bey,<sup>16</sup> and those of Levy,<sup>17</sup> show, moreover, that these salts exert a detrimental influence upon the growth of other organisms. In conditions, therefore, which simulate typhoid fever and in which organisms other than the typhoid bacillus may be present in the blood, our knowledge of the inhibitory influence of bile on certain bacteria (for instance the pneumococcus) makes it evident that a negative result might be obtained, whereas the use of the ordinary media may result in a positive finding. And, as we have seen, the

<sup>15</sup> *Centralbl. f. Bakt.*, 1907, vol. xliv, Heft 5.

<sup>16</sup> *Annales de l'Inst. Pasteur*, 1907, No. 1.

<sup>17</sup> *Virch. Arch.*, February, 1907, Heft 2.

ordinary media will also not interfere with the development of the typhoid bacillus.

I wish to draw particular attention to the use of 2 per cent. glucose agar.<sup>18</sup> This medium not only permits good growth of the typhoid bacillus and other organisms,<sup>19</sup> but the colonies of the typhoid bacillus develop in it in a characteristic way. The features of the colonies on the medium are as follows: They usually appear in the first twenty-four to thirty-six hours of incubation and are pinpoint in size, with a disproportionately wide area of green coloration around them. This areola is well defined at the circumference, and may be limited by a ring of darkened blood. The colonies show little tendency to increase in size for the first two or three days, whereas the surrounding green areola widens very rapidly. This description applies only to colonies of typhoid bacilli in the depths of the medium. The surface colonies also develop a green color, but they are much larger than the deep colonies and present nothing that may be considered characteristic.

The development of a green coloration about the colonies in the glucose blood medium is a feature that is not restricted to the typhoid bacillus itself; other bacteria may give rise to the same phenomenon. Ruediger<sup>20</sup> studied the question of the production of this pigmentation, and found that the pneumococcus, the streptococcus, *Staphylococcus aureus*, and the typhoid bacillus produce it; whereas, *Bacterium coli* does not, producing instead a rapid and diffuse hemolysis. From our experience, however, the only colonies that need to be considered from a differential standpoint are those of *Staphylococcus aureus*, *Bacterium coli*, and the para-colon group. *Staphylococcus aureus* grows usually in much larger and more disk-like colonies; and in addition to the green color which it produces, there develops within twenty-four to thirty-six hours a clear area (complete hemolysis) immediately around the colonies between the colony and the area of green coloration. The hemolytic ring may be very narrow and in the early stages of incubation may be entirely absent.

In one case of general infection by the colon bacillus, which we had the opportunity of studying, the colonies in the glucose medium developed to a much larger size within the given period than do colonies of the typhoid bacillus. They showed, moreover, a greater tendency to break through and spread out upon the surface of the medium, and produce gas. Gas bubbles were also produced by the paracolon bacillus, but the colonies otherwise resembled very closely those of the typhoid bacillus.

When, therefore, we find that stained smears from the colonies of

<sup>18</sup> Libman, loc. cit.

<sup>19</sup> Although this medium is better than the bile media for routine work, in connection with bacteria other than the typhoid bacillus, it is sometimes not as good as agar unless serum be added.

<sup>20</sup> Jour. Infect. Dis., September, 1907.



the type described as characteristic for the typhoid bacillus show the presence of a Gram-negative bacillus, we can safely place the organism in the typhoid-colon group.<sup>21</sup> Moreover, when colonies are present on this medium which do not correspond to the type described the presence of the typhoid bacillus may be excluded. The character of the colony which the typhoid bacillus produces on 2 per cent. glucose blood agar affords us then a great help in identifying the organism early. Most of our positive results on the glucose agar were obtained within twenty-four hours after taking the culture. In some instances the typical typhoid colony developed within sixteen hours. Delay in development of the colonies may at times be accounted for by errors in the titre of the medium.

Of the 154 cultures taken promiscuously, some for diagnosis and others for research, 110 gave growths of the typhoid bacillus and 2 of paracolon (so-called paratyphoid) bacilli. In 1 case of typhoid fever, complicated by pneumonia and otitis media, a streptococcus was obtained from the blood. The typhoid bacillus was no longer present (the Widal reaction was positive). In another case studied through the kindness of Dr. Eli Moschkowitz, both the typhoid bacillus and a streptococcus were found in the same culture. The results obtained with 2 per cent. glucose bouillon, 2 per cent. glucose agar, and ammonium oxalate solution were the most encouraging; so that our experience leads us to suggest the use of these three media for diagnostic work. As for the quantity of blood, it may be said that 2 c.c. is sufficient to give positive results in 80 to 85 per cent. of positive cases; but when a larger amount of blood can be withdrawn without inconvenience, it is desirable to obtain it, especially in the later weeks of the disease when the organisms are apt to be very few in number. It is necessary to draw attention to the fact that while the total percentage of our positive results is about the same as that given by other authors, more of our cases were studied during the third and fourth week, and as the results are generally considered to be better in the first and second week, the methods which we have decided to adopt for routine work seem to promise better results than the methods generally used.

## SUMMARY VI.

Week of disease.	No. of cultures.	Cultures positive.	Widal positive.
1 . . . . .	8	7 (88.5 per cent.)	2 ( 28.5 per cent.)
2 . . . . .	44	39 (88.6 " )	28 ( 63.5 " )
3 . . . . .	42	25 (60 " )	36 ( 86 " )
4 . . . . .	15	8 (53.3 " )	12 ( 80 " )
5 . . . . .	7	5 (71.5 " )	5 ( 71.5 " )
6 . . . . .	3	1 (33.3 " )	3 (100 " )
7 . . . . .	3	1 (33.3 " )	2 ( 66.6 " )
Total . . . . .	122	86 (70.5 " )	88 ( 72.1 " )

<sup>21</sup> All the bacilli isolated in our cases were, of course, further identified by the study of their cultural features and by the presence of agglutination with immune typhoid serum.

## SUMMARY VII. RELAPSES

Intercurrent relapses, 5—all positive.

Day of relapse.	No. of cases.	Result of culture positive.
2 . . . . .	5	3
3 . . . . .	5	4
4 . . . . .	2	1
5 . . . . .	4	4
6 . . . . .	2	2
7 . . . . .	2	1
11 . . . . .	1	1
12 . . . . .	1	0
14 . . . . .	1	0

The last two summaries permit us to draw certain deductions concerning the efficiency of the blood culture as a diagnostic means in that stage of the disease when other means are unavailing. They also draw our attention to the investigation of the relationship of the bacteremia to the course of the disease. As shown in Summary VI, and as already mentioned above, the results obtained agree in general with those of other investigators. The relationship of the positive blood culture and the positive Widal reaction has been studied by a number of authors. The statistics of Coleman and Buxton<sup>22</sup> show that many of the positive cultures antedate the presence of the Widal reaction. Ghaetghens<sup>23</sup> studies showed that of 917 Widal tests made, in the first week of the disease, 25 per cent. were negative, in the second, 10 per cent., and in the third, 4.7 per cent. He also found that in 140 cases in which the Widal reactions remained negative, 34 were diagnosed by positive blood cultures, an experience previously shared by a number of other observers. Our own results confirm the previous observations.

The lack of relationship between the result of the culture and the type and severity of the disease has also been noted by nearly all the writers who have reported on large series of cases. Although some fever is usually present at the time when the blood culture is positive, there is no direct dependence of the result upon the height of the temperature. A positive result may be obtained with the temperature at 100° F. as likely as at 105° or 106°, provided such a temperature occurs in the course of the active stage of the disease. A number of our cases yielded positive results shortly before defervescence; that is, within one, two, or three days, but in no cases was a positive result obtained after defervescence was established. Conradi's results in afebrile cases of the disease are certainly exceptional. Coleman and Buxton state that in cases with a long duration, the bacillus is in the blood as long as the temperature persists. My own results support this view in part only. We must distinguish in prolonged cases between those in which the prolongation is due to the fever alone, and those in which prolongation of the tempera-

<sup>22</sup> AMER. JOUR. MED. SCI., June, 1907.<sup>23</sup> Arbeiten aus dem k. Gesundheitsamte, 1907, Heft 1.

ture is due to some complication (such as phlebitis or bronchopneumonia, etc.). In the former group of prolonged cases positive results can be expected. The cases with intercurrent relapses may be regarded in the same group as the last mentioned. The five cultures of our series which were taken in such cases were all positive (Summary VII).

We have had the opportunity of studying 23 relapses; 16 of these gave positive results, approximately 70 per cent., a figure which is nearly the same as that given by a study of the primary attacks. Our experience with negative cultures during the afebrile period warrants the conclusion that in the relapse we are dealing not with the continuation of the original bacteremia, but a new bacteremia. In the intercurrent relapse it is possible that the bacteremia is continuous with the original bacteremia. In 4 of the 16 cases of relapse with positive results, negative results were obtained in the primary attack. An analysis of the results obtained on different days of relapse shows (although the series is too small as yet to be conclusive) that the results are better when the fever nears the fastigium than they are in the earlier days. In 1 case we had the opportunity of making cultures on the third, seventh, and eleventh days of a relapse. The first two cultures were negative, and the third positive. This observation also confirms the view expressed by Schottmüller, that in the true relapse there is a new invasion of the blood.

From a consideration of the results obtained by most investigators it appears to be certain that the bacteremia is concerned in the production of at least some of the clinical aspects of the disease. As Coleman and Buxton state, the number of positive cultures is such that one must conclude that the typhoid bacillus is present in the blood in every case of typhoid fever at some time or other. My own studies with the different media indicate that negative results in the early stages of the disease are accidental. These observations are important not only from the standpoint of etiological and pathological studies, but also from the standpoint of diagnosis, for they show that a continued fever (and this conclusion was drawn by Schottmüller and later by Libman<sup>24</sup>) which lasts for several days after the cultures have shown the blood to be free from typhoid bacilli is in all probability not that of typhoid fever.

To sum up, all the results hitherto obtained show that in typhoid fever there is a bacteremia which becomes progressively less marked as the disease goes on. Whether the cases which extend beyond the third, fourth, and fifth week and in which positive results are obtained are due to repeated invasions of the blood current or not, is a question which cannot at present be decided. From the present state of our knowledge it is difficult to formulate a definite view of the

<sup>24</sup> Trans New York Academy Medicine, March 7, 1907.

significance of the bacteremia in typhoid fever. The case recently published by Conradi<sup>26</sup> in which bacilli were present in the blood before the onset of the fever, and the case described by Widal, in which a positive blood culture was obtained on the second day of disease, would appear to lend strength to the view of Schottmüller concerning the close relation of the bacillemia to the fever. Certain facts presented by our own studies make us hesitant concerning the occurrence of bacillemia from the very inception of the disease, for in one case the culture taken on the fifth day was negative, and another culture taken a few days later was positive. In the second case, two cultures taken during a relapse were negative, and the third positive. We are in need of some studies of cases in which the blood cultures were made on the first or second day of the disease (or of the relapse).

Our studies do not warrant us in drawing any conclusions concerning the relation of the number of bacilli present to the prognosis of a given case. Schottmüller and Schueffner are of the belief that there is a relationship. Further studies in this direction are also desirable. It is not at all unlikely that the study of the biological differences of the organisms from the blood of different patients will throw some light on prognosis and therapy.

Our studies permit the following conclusions:

1. The bactericidal influence of the blood in typhoid fever in relation to the obtaining of positive results in the blood cultures has been overestimated. Great dilutions of the blood are not essential; a number of media will give good results.

2. The best results in our experience were obtained with the use of 2 per cent. glucose bouillon, 2 per cent. glucose agar, and ammonium oxalate solution.

3. On 2 per cent. glucose agar the typhoid bacillus grows in such a characteristic way that the presence of a certain type of colony on it is quite diagnostic, and the absence of such a colony points very strongly against the presence of the typhoid bacillus.

4. The bile media were not found to be as reliable as the media mentioned above.

5. The results presented are in agreement with those obtained by others. The total positive results obtained by us are in agreement with the results obtained by others, notwithstanding the fact that more of our cases were studied later in the course of the disease.

6. Although the maximum results are obtained in the first and second week, there is not sufficient proof as yet that the bacilli are present in the blood from the very inception of the fever.

7. Protracted cases yield positive results if the continuation of the fever is not due to complications (or starvation).

8. A continued fever lasting several days after the blood has been

shown to be free from typhoid bacilli will nearly always prove not to be a case of typhoid fever.

9. The results in relapses are the same as those in the primary attacks. The bacillemia in the relapses is due to a new invasion.

10. We cannot draw any definite conclusion, as yet, concerning the value of the blood cultures in determining the prognosis.

It is with a deep sense of gratitude that I wish to acknowledge my indebtedness to Dr. E. Libman for his advice and constant guidance in this work. To Drs. Hertz, Ryttenberg, and Fried, I wish to express my thanks for their kind assistance.

## THE UNCERTAIN RESULTS OF SUTURING NERVES.

BY GEORGE TULLY VAUGHAN, M.D.,

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WHEN one reads the reports of the numerous cases of nerve suture and observes the small percentage of successful results, he is forced to conclude either that the repair of nerves is uncertain and erratic, or that the technique of such operations is far from satisfactory. There certainly seems to be a difference in the ability of different nerves to regenerate. Contrast, for example, the perverse persistence of the trifacial in reproducing itself after the removal of segments as much as one inch in length with the obstinate resistance to reunion or regeneration of the median or ulnar nerve after it has been carefully sutured together and apparently placed in the most favorable condition for repair.

Whether regeneration of nerves occurs as an outgrowth from the neuron or central nerve cell, according to Waller, Ranvier, His, Waldeyer, and others, or whether, according to Bethe, Nissl, Dohm, Ballance and Stewart, and Tizzoni and Cattani, the regeneration is the result of proliferation of the cells in the sheath of Schwann, is a matter which has not been decided, but the latter theory seems to be gaining ground.

It is generally thought that immediate suture of a divided nerve is more likely to be successful than secondary suture, but this seems to be a matter of no importance, according to Bowlby.<sup>1</sup> Thus, in 81 cases of primary nerve suture there were 32 successful results, 34 partially successful, and 14 failures, while in 73 cases of secondary nerve suture there were 32 successful results, 26 partially successful, and 15 failures—the primary suture giving 39 per cent. of successes and the secondary 43 per cent. of successes. Powers<sup>2</sup> reviews 22 cases of nerve grafting in which a segment of a nerve from a dog or

<sup>1</sup> An American Text-book of Surgery.

<sup>2</sup> Trans. Amer. Surg. Assoc., 1904.

from some other source was transplanted between the two ends of a severed nerve, with 3 "good" results and 3 "fair" results, 27 per cent. being more or less successful, although Powers says, "One is forced to question the authenticity of some of the results accounted 'satisfactory,'" and concludes by expressing the opinion that nerve transplantation should be discarded. Powers reviews also 11 cases of flap operations, in which a flap was turned down from one or both ends in order to bridge the gap, with 4 complete or partial successes, 2 failures, and 5 discarded as having been reported too early or as lacking in detail; 10 cases of implantation or anastomosis, in which one nerve was implanted into another, with about 50 per cent. of "encouraging" results; 7 cases of bone resection, but does not give results; 5 cases of suture à distance, with encouraging results; and one case of tubulization.

Murphy<sup>3</sup> gives the following: Implantation for poliomyelitis, 11 cases, 1 success, 6 improvements, 1 failure, 3 too early to know the result; for facial paralysis, 33 cases (including 2 of tic convulsif); 21 of faciospinal-accessory and 12 of faciohypoglossal, with 7 successes, 15 improvements, 5 failures, 1 lost sight of, 1 indefinite, 4 too recent to give definite result, but some had improved. Seven had associated movements of the shoulder or tongue. Of the 7 successful cases, 5 were faciospinal-accessory and 2 were faciohypoglossal.

Of operations for rupture of the brachial plexus, A. S. Taylor<sup>4</sup> reports 9 cases with 1 death, and improvement in some cases; but he does not state in how many or to what extent.

Thus, it is seen that the percentage of successes is small even in a large number of operations. It is true that some of the cases were reported too early to know what the final results would be, but this may be offset by the number of eventual failures which are never reported—the inducement to publish failures not being very great.

CASE I.—*Wound by a saw dividing the radius, the median and the radial nerves, and most of the tendons of the wrist; suture of the divided structures.*

C. D., a white boy, aged fifteen years, was admitted to the Emergency Hospital, March 30, 1898, on account of a wound received the day before by a circular saw striking the right forearm just above the wrist. The wound had been temporarily closed and the patient was sent to the hospital for the purpose of having the hand amputated.

On opening the wound and examining the parts, the following conditions were found: Fracture of the radius about 2 inches above the wrist-joint and division of the median and radial nerves, the radial artery, and the tendons of the flexor carpi radialis, palmaris longus, flexor sublimis digitorum, part of the flexor profundus

<sup>3</sup> Surgery, Gynecology, and Obstetrics, April, 1907.

<sup>4</sup> Jour. Amer. Med. Assoc., January 12, 1907.

digitorum, the flexor longus pollicis, the extensor ossis metacarpi pollicis, extensor primi internodii pollicis, extensor secundi internodii pollicis, supinator longus, extensor carpi radialis longior, and extensor carpi radialis brevior. The median nerve was carefully united with fine silk, using through and through sutures, and all the divided structures except the radial nerve and the flexor longus pollicis were united, although it was not certain that in every case the two ends which were united were those which belonged together. The wound suppurated but finally healed, and the patient seemed to be getting pretty good use of his hand at the end of about two months, when he disappeared, and was next seen April 13, 1906, eight years after the injury. A large scar is seen above the wrist, which is exquisitely tender over the middle of the anterior surface. The hand is slightly flexed at the wrist and slightly deviated toward the ulnar side. He has good use and sensation of all the fingers except the index finger and thumb, which are numb to pin pricks on both dorsal and palmar surfaces; cannot flex the index finger or thumb, but can hold objects between the index finger and thumb by a curious trick—he catches the index with the middle finger and brings it down against the thumb; cannot appose thumb to fingers. It is a good useful hand for rough work, although it is evident that the median nerve is still ununited and one end is probably indicated by the tender point in the scar. The patient is not willing to have another operation to free the median nerve from the scar in which it seems to be embedded.

*CASE II.—Gunshot wound of the right arm, severing the median nerve, brachial artery, basilic vein, and the biceps and coracobrachialis muscles; nerve sutured.*

October 19, 1902, N. E. M., a white male, aged thirty-four years, a clerk, was admitted to Georgetown University Hospital, having just been wounded while holding a gun in his hand, the load of birdshot passing through the right arm just below the middle and dividing the median nerve, the brachial artery and veins, the basilic vein, and the biceps and coracobrachialis muscles. The ulnar nerve was stripped bare for a space of two or two and one-half inches, but did not seem to be wounded. There was little hemorrhage, the ends of the brachial artery being filled with coagula.

The ends of the median nerve were united with two silk sutures at right angles to one another, passing entirely through the nerve, the muscles were sewed together with catgut, and the brachial artery ligated with catgut. For a month there was almost complete paralysis of the flexor muscles of the hand, showing that the ulnar nerve had suffered from contusion or concussion.

The bone had been injured by the shot, and a sinus formed which discharged pus several months before healing. It took the patient more than six months to recover the use of the muscles supplied by the ulnar nerve, and he has never recovered the use of those supplied

by the median nerve. Examined July 29, 1904, more than eighteen months after the injury, the following notes were made: Sensation seems normal to pin prick except over back of last phalanx of middle finger; pronation and supination normal; good strong flexion and extension of the three inner fingers, but not quite perfect, the last phalanges not being completely flexed nor completely extended. The index finger is capable of only about half flexion, and the thumb can be flexed only to a very slight degree and cannot be opposed to the other fingers. Still the patient has good use of the hand as salesman in a shoe store, and is unwilling to have another operation for the purpose of improving the condition of the hand.

Evidently in this patient the median nerve has not united, or, if so, the point of union is occupied by scar tissue which interrupts the continuity of the axis cylinders.

The patient was again examined September 5, 1907, and his condition was found to be unchanged.

*CASE III.—Gunshot wound of the left arm, dividing the median nerve and the brachial artery; flap method used in suturing the nerve.*

F. W., a colored male, aged sixteen years, was admitted to the Emergency Hospital June 7, 1904, on account of a gunshot wound received the day before. The charge of small shot from the gun, almost touching the patient's body, passed along the left side, tearing the flesh from the seventh, eighth, and ninth ribs, opening the pleural cavity, then striking the left arm on the inner side about midway between the elbow and shoulder, it passed upward and backward, to emerge posteriorly about one and one-half inches above the wound of entrance.

The patient's condition did not justify the operation for suturing the nerves until July 2, four weeks after the receipt of the wound. From the symptoms it was assumed that the median nerve and brachial artery had been divided. There was inability to close the fingers completely, the thumb and index finger could not be flexed at all, the three other fingers could be flexed partially, the little finger almost perfectly, the ring finger not quite so well, and the middle finger still less. After closing the fingers he had difficulty in extending them. Sensation seemed unimpaired except over the last two phalanges of the middle finger, both dorsal and palmar surfaces. Pronation and supination were possible, and the patient could touch the tip of the middle finger with that of the thumb, but none of the others. While resting quietly the left index finger lay straight, with almost continual successive contractions of the extensor tendon.

Under ether the wound in the arm, partially cicatrized, was enlarged, exposing the lower segment of the median nerve, which was in its normal position by the side of the obliterated brachial artery. After a little search the upper segment was found pointing backward and lying in the upper part of the wound of exit. The two segments could not be approximated—at least an inch of the nerve had been



destroyed. A flap was cut from the upper segment, turned down, and sewed end-to-end to the lower segment with silk—one through and through suture and several in the neurilemma. The other nerves showed no sign of injury.

The wound healed and the patient left the hospital before any change had taken place in the hand.

November 20, 1907. Beyond slight numbness in the thumb and first two fingers, the result is perfect. Flexion and extension, apposition of the thumb to the tips of the fingers, pronation and supination, all are normal. The radial pulse is about as strong in the left wrist as in the right.

There is a suppurating sinus leading to the left pleural cavity. After leaving the hospital, while the wound in the side was still discharging, the physician one day while probing the wound removed from its interior a one-dollar bill, which had been carried from the patient's pocket into the tissues by the charge from the gun.

*CASE IV.—Wound with broken glass dividing the median nerve and several tendons in the wrist; suture of the divided structures.*

A. C., a white female, aged six years, was admitted to Georgetown University Hospital, December 31, 1904, having just had her right wrist cut with broken glass. Examination showed an oblique, clean-cut wound across the anterior surface of the wrist joint, not reaching quite across the radial side, from which the end of a tendon protruded. The patient was asked to flex the fingers, and at first said she could not do it, but finally did so, slowly flexing the four fingers until their tips touched the palm, but the second and third phalanges were no well flexed. Other tests could not be satisfactorily made, as the child was frightened.

Under chloroform it was found that the median nerve, all four tendons of the flexor sublimis digitorum, and the flexor profundus digitorum had been completely divided, while the flexor carpi radialis had been partially divided. The upper ends of the tendons had retracted from half to one inch and were found by splitting the skin and fascia from the wound upward. All were united, using the same kind of suture for nerve and tendons—silk through and through—and other sutures for the sheath. Profuse suppuration followed, but the wound healed in about four weeks.

Examination March 3, two months and three days after the injury: flexion of fingers about the same, second and third phalanges do not flex completely; most marked in the index finger. The thumb can be approximated to the other fingers with some difficulty, which is greatest with the little finger. There is some numbness of the thumb, index, and middle fingers.

The patient was again examined March 31, 1907, two years and three months after the injury, and the hand was found perfectly normal.

In this patient the flexion of the first phalanges by the interossei

muscles, which are supplied by the ulnar nerve, was beautifully shown, as, although both flexor tendons were completely divided, the patient could still close the fingers, it is true in a loose sort of way, but a careless observer would probably have concluded that the flexor tendons had not been injured.

The ability to approximate the thumb to the fingers must be explained, it seems to me, on the ground that the adductors and part of the short flexor of the thumb, which are supplied by the ulnar nerve, act to some extent for the opponens pollicis, but that such substitution does not always take place is shown by the result in the second case reported.

*CASE V.—Saw wound of the axilla dividing the axillary vessels and the median, ulnar, musculospiral, and internal cutaneous nerves; suture of the nerves; gangrene; amputation below the elbow.*

A. S., a white male, aged eighteen years, was admitted to the Emergency Hospital July 7, 1907, having the day before been thrown against a circular saw. Examination showed a large ragged wound of the right axilla and right side of the chest, extending to, and grooving the neck of, the humerus and dividing the pectoralis major, the axillary vessels, and the median, ulnar, musculospiral, internal cutaneous, and lesser internal cutaneous nerves. The vessels had been closed by the formation of thrombi. The nerves were united after considerable difficulty in finding the ends and determining which ends belonged together, using silk and overlapping the ends.

The lower ends of the median and musculospiral nerves were concealed several inches below the wound, and dissection of the arm below the wound was necessary in order to find them. The wound was partially closed and drainage provided. Next day the hand was cool, and slight gangrene of the edge of the wound was noticed.

July 16, a line of demarcation had formed about the middle of the forearm, so that the forearm was amputated about three inches below the elbow. Recovery followed, but it is too early to expect any restoration of function in the muscles supplied by the sutured nerves.

## THE PATHOGENESIS OF TABES DORSALIS.<sup>1</sup>

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THE pathogenesis of tabes dorsalis has excited a great deal of discussion ever since Duchenne<sup>2</sup> first differentiated the locomotor

<sup>1</sup> Read by invitation at a meeting of the Philadelphia Neurological Society, February 24, 1908.

<sup>2</sup> Arch. de méd., 1858.

ataxia he so well describes. None of the more recent reviews of the subject has formulated very definite conclusions, nor acceded categorically to a single theory; none of the framers of these has quite succeeded in accounting for all the clinical facts already ascertained. Having had exceptional opportunities during the last two years to examine the preparations of many observers and to study a very large number of cases of tabes fruste, I wish in this presentation to indicate, as briefly as possible, the reasons for the conclusion reached that in the main the true explanation is that of Nageotte.<sup>3</sup> An attempt is made also to account for the discrepancies between the findings of others and those of Nageotte's remarkable studies upon the radicular nerve.

Avoiding all arbitrary divisions, types, and stages of disease, and sketching as far as possible the processes which occur and the evolution of the symptoms, I postulate in the first place, with the great majority of neurologists, that the tabetic process differs not in kind, but only in locality from the paralytic process, and in the second place I reject the explanation, familiar in the text-book, that tabes is a primary dystrophy either of the posterior column or of the sensory protoneuron as a whole or an atrophy thereof, directly caused by alcohol, prolonged strain, syphilis, or sexual excesses. To make this clear a few anatomical and physiological details must be recalled.

THE LESIONS ON THE POSTERIOR ROOTS.—It will be recollected that in or near the row of foramina between the laminae of the vertebrae are situated the ganglia upon the posterior roots of the spinal cord, and that the lower ganglia are a considerable distance inside the spinal canal. The nutrition function of the ganglion cells is too well known to require emphasis. But it is perhaps insufficiently borne in mind that the regenerative function of these cells is efficacious only when the fiber concerned possesses a neurilemma, and that within the spinal cord the axons of the root nerves lose this sheath, retaining only the white substance of Schwann.

Between the lower ganglia and the segment of the spinal cord corresponding with each there intervenes several inches, which the radicular nerve traverses in contact with the leptomeninges, which arrangement is shown in Fig. 1. This shows clearly the canal formed by the pachymeningeal reflection as the nerve pierces the theca vertebralis to become peripheral. In this canal it is probable that communication takes place between the cerebrospinal fluid filling it and the lymph in the sheath of the peripheral nerve (Orr and Rows<sup>4</sup>). Figs. 2, 3, 4, 5, and 6, show the lesions

<sup>3</sup> Soc. de Biol., January, 1901; July, November, December, 1902; July, 1904; May, October, 1905; January, 1906. Note sur les formations cavitatives par perinévríte dans les nerfs radiculaires, *Rev. neur.*, 1907. Sur la systematisation dans les affections du système nerveux et en particulier dans le tabes, Congrès Neur. de Paris, 1900. *Neuv. Icon. Salpet.*, 1904, p. 1. Pathogénie du Tabes Dorsalis, Paris, 1903. *Rev. neur.*, 1906; January, 1903.

<sup>4</sup> *Rev. Neur. and Psy.*, 1903, p. 639; 1906, p. 25; 1907, p. 346. *Brain*, 1904, p. 460.

described by Nageotte in this locality in cases of tabes and tabo-paralysis. Examination shows this lesion in all stages from simple

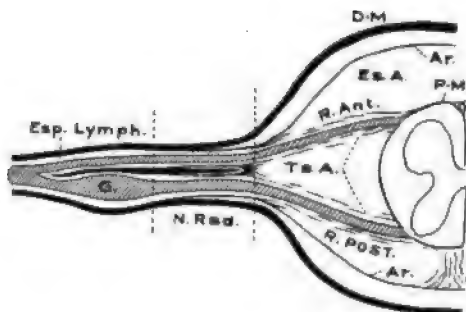


FIG. 1.—Diagram showing the relations of the meninges to the radicular nerve. *N.Rad.*, radicular nerve; *PM*, pia mater; *Ar*, arachnoid; *DM*, dura mater; *R.Ant.*, anterior roots; *R.Post.*, posterior root; *G*, ganglion; *E.L.*, facultative lymphatic space. (From Nageotte.)

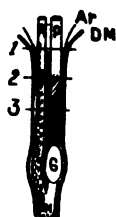


FIG. 2.—*AP*, anterior and posterior roots; *Ar*, arachnoid; *DM*, dura mater; *G*, intervertebral ganglion. (From Nageotte.)

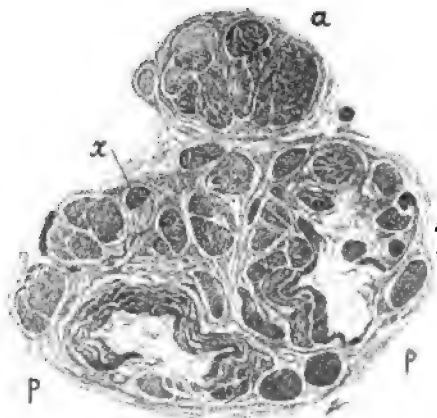


FIG. 3.—Cross-section of the radicular nerve in a general paralytic in which the lesions of the anterior root (*a*) were more prominent than those of the posterior root (*p*). The section is at line 3 of Fig. 2 in which the posterior root is involved also. Note the perineuritis with its cavity formation, and the paler bundles of degenerated fibres even where there is no perineuritis. The bundle *x* is half intact. (From Nageotte.)

round-cell infiltration, through granuloma, toward necrosis with cavity formation. They are the fruit of complete serial sections of several radicular nerves in each of eleven cases of this disease.

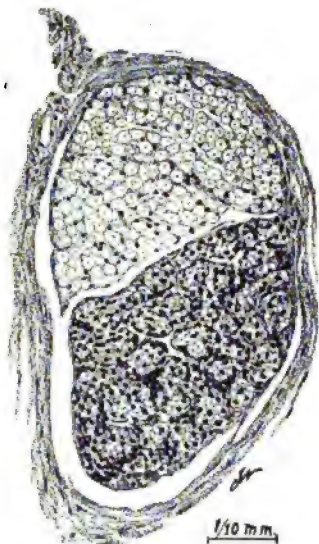


FIG. 4.—The region *x* in Fig. 3 magnified 90 diameters to show the healthy fibers and those from which the myelin has disappeared. (From Nageotte.)

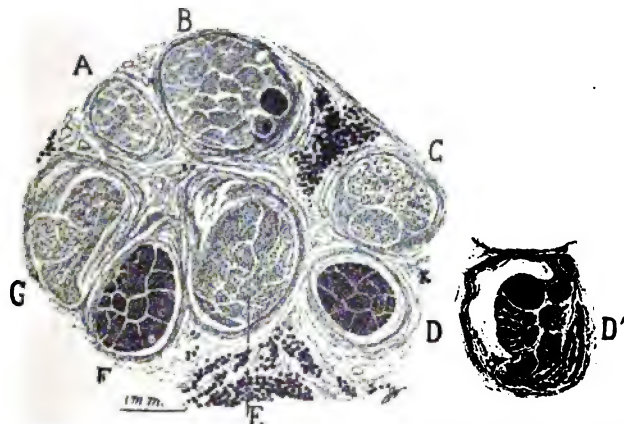


FIG. 5.—Cross-section of the radicular nerve in a tabetic, showing the round-cell infiltration. The bundles *F* and *D* are spared, while all the rest are degenerated. *D'* is a cross-section of *D* lower down. Notice the area of lacunar perineuritis which displaces some fasciculi. Lower still this necrosis was found to occupy the centre of the bundle. (From Nageotte.)

Now, even the chronicity of the infection and the comparatively indolent reaction of the granulomatous process are in this situation sufficient to affect seriously the nerve fibers contiguous to the in-

flammatory area; for in the circumscribed canal of unyielding dura mater, the pressure of toxic effects of the exudate impinges upon the nerve fibers surrounding. These are either destroyed, or at least sufficiently injured to prevent the passage of the impulses from the ganglion cell, which subserves the trophicity of the distal portion of the fiber, which accordingly degenerates. Their lack of neurilemma prevents their regeneration, even after the granuloma has undergone absorption; and the postmortem appearance of tabes dorsalis is thus constituted. Regeneration, however, does occur in the posterior root itself just as far as Obersteiner's ring; and it is to this cause that we must attribute the many attempts to refer the tabetic process to a primary dystrophy; for the earlier pathologists had not conceived that what appeared a healthy structure, was the real source of the lesion which they found in the posterior column of the spinal cord.

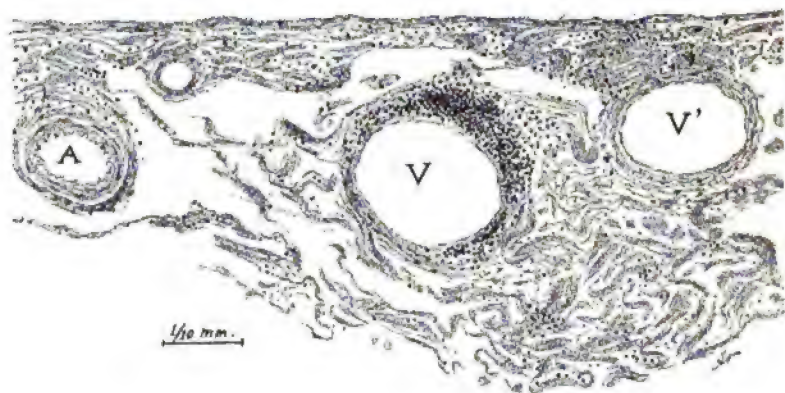


FIG. 6.—An area of old meningitis in a tabetic. The process is in resolution except around V, where an inflammatory nodule is in full development. Note the sclerotic atrophy of the walls of the artery A and veins V and V'. (From Nageotte.)

Nageotte's opinion that the process is toxic does not accord with the findings of similar posterior column degenerations with evidence of pressure upon the roots, in cases of cerebral tumor (Lejonne<sup>5</sup>) in which the manometric pressure of the spinal fluid is increased; and it would seem that the mechanical factor of the granulosomatous infiltration was enough to account for the tabes, although the experiments of Orr and Rows show that causes purely toxic may produce degenerative changes.

**THE DISPARATE DISTRIBUTION OF THE LESIONS.**—The preponderance of the process upon the fibers of deep sensibility is connoted by the name given to the disease by Duchenne, of Boulogne, locomotor ataxia. Its occurrence may be due to as yet unascertained peculiarities in the course of these fibers, which we

<sup>5</sup> L'Encéphale, March, 1907.

know to accompany the motor nerves. A search among carefully described cases of tabes, however, shows that other anomalies of sensation are very much commoner than the classics allow; it is probable, therefore, that it is merely the inconvenience entailed by the impairment of this function which is the cause of the stress laid upon its involvement when the pathology of tabes is considered.

Figs. 3 and 4 show how disparate is the involvement of the fasciculi composing the radicular nerve. Whether this is due to an elective affinity of a toxin for a particular sensory system, or whether it is due to an accidental incidence depending on the local differences of arrangement, cannot be affirmed with certainty. Clinical evidence seems to indicate that some of the fibers subserving the sensation of cold are spared relatively long; but no accurate data yet exist to indicate whether these fibers belong to the protopathic or epicritic systems demarcated by Head.<sup>6</sup>

The fibers subserving the sense of attitudes and those of deep pain are considered to be particularly early affected; and Marinesco<sup>7</sup> has shown that the former is generally associated with the appreciation of vibration, which is much impaired in the course of tabes.

THE DISSOCIATION OF THE SENSIBILITY; THE CAUSES OF THIS.—Head has shown that these are two functions of deep fibers accompanying motor nerves. Spacing sense, thought by him to be in part a function of the same system, has not yet been sufficiently investigated in tabetics; but the implication of the two foregoing shows that the lesion must be one of the peripheral sensory neurons; for these two modalities of sensation become dissociated in the spinal cord, and would require two separate lesions for their implication, sense of position and movement passing homolaterally in the posterior column, while deep pain joins superficial pain to pass heterolaterally in a portion of Gowers' tract (Page May<sup>8</sup>). Touch and deep pressure impulses are, on the other hand, amalgamated into a single path as soon as they reach their relay neuron in the spinal cord. They mount cephalad in a heterolateral tract in the neighborhood of the ventral horn. Thus, if a lesion situated in the cord prevents the passage of impulses of deep pressure, it necessarily prevents the passage of tactile cutaneous impulses also, whether these are epicritic or protopathic, these distinctions being solely peripheral as regards their topographical separation (Head and Thompson<sup>9</sup>).

The disparate character of the sensory troubles is shown in "tabes supérieure" and by such cases of radicular astereognosis as were described by Déjerine<sup>10</sup> and Noica and Averamescu,<sup>11</sup> of Bucarest,

<sup>6</sup> The Consequence of Injury to the Peripheral Nerve in Man, *Brain*, 1905, xxviii, 116.

<sup>7</sup> *Semaine méd.*, 1905, xxv, 565. *Rev. neur.*, 1907.

<sup>8</sup> The Afferent Path, *Brain*, 1906.

<sup>9</sup> The Grouping of Afferent Impulses within the Cord and Brain, 1905.

<sup>10</sup> *Rev. neur.*, 1904.

<sup>11</sup> *Ibid.*, 1906, p. 99.

in which the palmar side and corresponding fingers could not identify the bodies palpated.

As other examples of such irregular incidence, the case cited by Dupré and Camus<sup>13</sup> and Camus and Sezary<sup>14</sup> may be cited. A most demonstrative case was that of Babinski and Nageotte,<sup>15</sup> in which the patellar reflex had persisted until death. Postmortem, it was found that the middle root zones were much less affected than the posterior root zones, while the reflex collaterals and the vertical fasciculus of the posterior horn were relatively conserved. This greater implication of the long fibers is, according to Nageotte, rather the exception. He bases this opinion principally upon the marked involvement of the external bandalette of Pierret, which he believes to be a tract of short fibers going to the column of Clark and not furnishing fibers to the column of Goll at all. These he believes to pass in the posterior external field, and perhaps the lower ones in Flechsig's oval. Raymond's<sup>16</sup> case, too, is striking in this regard, as all deep reflexes were retained. Although hypotonia usually accompanies the lost tendon reflexes, yet even these are sometimes dissociated, as in this case. It would appear, too, that the hypertonic muscles of the tabetic may become even spastic, either by involvement of the pyramidal tract, as in so-called *tabes combinée* (Noica<sup>17</sup>) or by the development of paralysis agitans, as in the case of Bychowski.<sup>17</sup> Reflexes too, may persist for some time although there is grave disorganization of afferent fibers from muscle, tendon, and joint, as evidenced by great muscular incoördination and lost sense of attitudes.

It is a pity that the two cases reported by Long<sup>18</sup> were not examined as regards the vestibular nerve; for the preservation of the patellar reflexes was there combined with great ataxia; and yet postmortem, very little change was found in the lower spinal cord or roots.

The beautiful description by Gowers<sup>19</sup> of the varying character of the lightning pains well shows the irregularity with which the fibers are attacked in the posterior roots; though his interpretation is inconsistent with the pathology for which this paper contends; for instance. "The superficial pains seem to be on the surface or just beneath the surface. They are usually felt at one spot, often only a few inches in extent, sometimes larger, extending down part of a limb, on the ears, on the face and especially about the mouth." "The pain is usually extremely brief, a stab or flash of pain, gone as soon as felt, but recurring." "These superficial pains have one remarkable effect; they make the skin tender. After they have

<sup>13</sup> *Rev. neur.*, 1902.

<sup>14</sup> *Soc. de Biol de Paris*, 1905.

<sup>15</sup> *L'Etat des reflexes tendineux dans le tabes compliquée de hémiplegie*, *Jour. de neurol.*, 1907.

<sup>17</sup> *Neurol. Zentralb.*, 1904, p. 786.

<sup>18</sup> *The Pains of Tabes*, *Brit. Med. Jour.*, 1905, i, 1.

<sup>13</sup> *Ibid.*, 1906, p. 1174.

<sup>14</sup> *Rev. neur.*, 1906, p. 1182.

<sup>18</sup> *Congrès de Genève*, 1907.



occurred a few times, sometimes almost as soon as they begin, the skin in that area becomes so tender that if touched the patient feels as if the place was an open sore. If the finger is drawn gently over it, the pain produced is often hardly bearable. A remarkable fact is that this occurs where sensibility to pain is lost." This description concords with that of the destruction or irritation of protopathic sensation: "the prick of a pin may occasion no pain whatever" (Head). Of the deep pains, the radicular character is as manifest; *e.g.*, "Pain after pain occurs at the same part, separated by a short interval." It is sometimes described as "like the pain of cramp when there is no muscular contraction." Of the girdle sensation, Gowers says that when superficial it is often accompanied by hyperesthesia, but when deep is without corresponding changes in the skin. Gowers also points out its occasional unilateral character.

The paresthesiæ are an endless list, and false interpretations are very probably due to the different degree of involvement of deep and epicritic fibers. His case of tabetic neuralgia without loss of the knee-jerks is a striking confirmation of this point of view; for the pains were entirely superficial; he could not bear the prick of a pin, but the sensation to touch was perfect. What is this but a protopathic paresthesia? There were five similar cases, all thus characteristic of root pain. Now, reference to Head's cases and those described by Lebar<sup>20</sup> will show that hyperesthesia of this nature is not due, as Gowers<sup>21</sup> thinks, to irritation in periphery, but in nerve trunk. The nutritional changes also confirm Nageotte's point of view.

In one case a cutaneous erythema with numerous small white spots accompanied the pain;<sup>22</sup> in one, the localized pain of the scalp was followed after a week by bending and breaking of the hairs about an eighth of an inch from their emergence. These phenomena conform to the trophic ones which Head<sup>23</sup> considers as dependent upon protopathic fibers.

The radicular distribution of the trophic changes is not consistent with their peripheral origin. The resemblance, too, of the arthropathy and osteopathy to those of syringomyelia is striking; but in the latter case the lesion affects the vasor centres in the intermediolateral column, and possibly certain other root fibers also; whereas, in the tabetic process it is the conducting fibers alone which are involved. The effect, however, does not differ. That these dystrophies are dependent upon the interruption of afferent impulses is, however, shown by the disappearance of the perforating ulcers when rest to the limb is enforced for a few weeks. It is only then that the ulcer can be adequately protected from the unfelt traumas which interfere

<sup>20</sup> Thèse de Paris, 1906.

<sup>21</sup> On the Nature of Tabes, Brit. Med. Jour., 1905, p. 57.

<sup>22</sup> The Dystrophies in Tabes, Brit. Med. Jour., 1906, p. 1267.

<sup>23</sup> The Afferent Nervous System from a New Aspect, Brain, 1905.

with its healing. Such an exposed surface would normally be so painful that the patient would be compelled to rest; but the painless mal perforante offers no inducement to this.

One of the hitherto unrecognized paresthesiæ is pruritis. Its characters, as pointed out by Lamy<sup>24</sup> and Millian<sup>25</sup> strikingly exemplify the irregular incidence of the tabetic process; for though generally bilateral, it may be confined to one side, and it usually coincides with a segmental area presenting other symptoms such as hypo-esthesia, or visceral crises. It naturally occurs only during the earlier stages of the disease.

The researches of Sherrington<sup>26</sup> and others have shown that the motor nerves of the anatomist are also accompanied by sensory fibers. These fibers proceed from end organs within the substance of the muscles, known as the muscle spindles. These spindles are sensitive to the deformation they undergo upon contraction of the muscles. It is possible that they are more exposed to noxious meningeal influences than other fibers which preceed straight into the posterior root. This perhaps explains the frequency of their involvement in the meningeal inflammation which leads to tabes dorsalis; though unpublished researches of Ransome, kindly communicated to me by Dr. Donaldson of the Wistar Institute of Anatomy, show that in rats at least these fibers are well mixed with those of cutaneous sensation by the time they reach the spinal ganglion. (See also Ingbert<sup>27</sup>). When the clinician investigates the loss of deep pain by pressing the ulnar nerve behind the elbow, pinching the Achilles tendon or faradizing the sural muscles, he is ascertaining the diminution of a function conveyed by these same nerves. Each of these symptoms is very common (90 per cent., Déjérine<sup>28</sup>) quite early in the disease.

As a matter of fact, other fibers are not spared; and if the disease is not arrested or cured or ended by death, all forms of sensibility are destroyed. The disease, however, progresses very slowly in most cases, although some rapid cases have been mistaken for acute myelitis, just as fulminating phthisis has for croupous pneumonia. As in tuberculosis, the individual lesions tend toward arrest, while the process tends to progress, the rate varying with the individual and the circumstances.

**THE MUSCULAR ATROPHIES.**—This tendency to local arrest explains the infrequency of serious myopathies; for Nageotte has shown that the anterior roots often degenerate. The possibility of their regeneration has not been generally accepted. But these and other cases, as well as the regeneration of the posterior roots, definitely shown by Bickles<sup>29</sup> experiments should compel the most

<sup>24</sup> Soc. méd. des hôp. de Paris, 1015.

<sup>25</sup> Ibid., 991.

<sup>26</sup> Jour. Physiol., 1894, xxv.

<sup>27</sup> Jour. comp. neurol., vol. xiii, No. 11.

<sup>28</sup> Semeiologie du système nerveux, Traité de Path. Gén. de Bouchard et Brissaud, 1904.

<sup>29</sup> Ueber das Verhalten des proximalsten (extramedullaren und pialen) Teiles der hinteren Wurzeln bei Degeneration und Regeneration, Neurol. Centralb., 1907, xx.

recalcitrant to accept the evidence of Nageotte's preparations as regards the anterior roots.

Muscular atrophy, however, is much commoner in tabes than earlier writers allowed. Witness the cases of Déjérine,<sup>30</sup> Souques,<sup>31</sup> Marie,<sup>32</sup> Oddo,<sup>33</sup> Camp,<sup>34</sup> and Raymond.<sup>35</sup> Nageotte's case of Aran-Duchenne palsy in a syphilitic, ataxic in the evenings, in which the patellar reflexes had disappeared, but who showed photomotor reflex irdoplegia and lymphocytosis, and whose symptoms began with ulnar neuralgia, is undoubtedly a tabetic, though the muscular atrophy may of course be of independent causation.

The recollection of the pathological principle upon which this depends would have saved many from their undue skepticism in this regard. It is sufficiently well known that nerves possessing a neurilemma will regenerate when no longer shut off from their trophic centre.

**WHY THE ANTERIOR ROOTS REGENERATE EFFECTIVELY.**—The trophic centre of the anterior root is the pyramidal cells in the anterior horn. Upon the absorption of the meningeal exudation which has interrupted that influence, they push out new fibers, which Nageotte has figured, and these, finding no interruption, wend their way once more to the muscular fibers which they innervate.

**WHY THE POSTERIOR ROOTS DO NOT REGENERATE.**—In the posterior root on the other hand, the portion of the fiber distal from its trophic centre, the spinal ganglion, loses its neurilemma on entering the central nervous system. Having suffered degeneration through the meningeal exudation upon the posterior root, that is, between itself and its trophic centre, its want of neurilemma deprives it of the power to regenerate, even when the trophic centre regains access; for the regenerating fibers, as Bickles' experiments show, stop short at the point of reflection of the pia mater at Obersteiner's ring (Fig. 7). Hence from the effects of this lesion no recovery is possible; but permanent disability through muscular atrophy due to anterior root lesions occurs only when the inflammatory exudation has eventuated in cicatrization.

Although I am one of the last to minimize the importance of the psychic factor in the temporary abasiæ of the tabetic, yet I believe that the future will show that these are sometimes, in part at least, due to the evanescent peripheral neuron palsies induced in the manner described. Faure<sup>36</sup> has already shown that ataxia of the trunk muscles is the real cause of some cases of tabetic abasia which were supposed to be psychic.

<sup>30</sup> Rev. neur., 1905, p. 1218.

<sup>31</sup> Atrophie musculaire dans le tabes, Rev. neur., 1907.

<sup>32</sup> Rev. neur., 1905, p. 146.

<sup>33</sup> Muscular Atrophy in Tabes, Univ. Penna. Med. Bull., 1905.

<sup>34</sup> L'Encéphale, 1907, p. 225.

<sup>35</sup> Congrès de Lille, 1906.

<sup>36</sup> Ibid., 1906, p. 587.

**REFUTATION OF OBJECTIVES TO THESE VIEWS.**—David Ferrier<sup>27</sup> has summarized the objections to these interpretations of the pathology of tabes dorsalis by stating that the meningitis postulated is not a constant phenomenon, being more frequently absent than present, and when existing, being more of a secondary thickening than an inflammatory process. These objections are completely refuted by the cytological data of lumbar puncture. That lymphocytosis signifies meningeal inflammation, no one disputes. The frequent postmortem findings of thickenings rather than inflammations is explained by the law of fibrosis of individual lesions in the history of granulomas, the process itself continuing in other parts.



FIG. 7.—Showing the point at which the fibers of the radicular nerve lose their neurilemma. This is outside the cord. The degeneration shown is due to the passage of toxic lymph from a peripheral focus. (Marchi.) (From Orr and Rows.)

Ferrier further objects that in tabes well-marked intramedullary degeneration is often unaccompanied by neuritis or atrophy of the posterior roots. The experiments of Bickles effectively answer this objection, as previously indicated. Ferrier declares unintelligible what he terms the practical escape of the anterior roots, and thinks it contradicts the usual law of the greater involvement of the motor fibers in neuritis of mixed nerves.

This so-called law is an imagination of clinicians, as no one who has studied alcoholic neuritis can doubt; for in this affection of mixed nerves the motor fibers sometimes escape entirely. The fact that the motor neuron is involved in plumbism, often to the exclusion

<sup>27</sup> Brit. Med. Jour., 1906.

of the sensory, is due to its greater susceptibility to that particular toxin. Pharmacological studies show the existence of these selective powers. Ferrier, too, declares that it is extremely rare for meningitis to produce intraspinal degeneration by implication of the spinal roots. This statement is contradicted by the examination of cases of Potts' disease (Alquier,<sup>38</sup>) spinal tumors, etc. Another argument he invokes is the segmental character of tabetic degeneration; but as segmental is a term in this connection convertible with radicular, the logic of this objection is not evident.

Another objection, its symmetrical character, does not accord with the facts, for Babinski<sup>39</sup> and Déjérine<sup>40</sup> have shown that in the early stages a relative asymmetry is an important character in the tabetic process.

Another objection is the occurrence of degeneration elsewhere, as in cranial nerves, ciliary ganglion, and sympathetic system. The cranial nerve affections are, of course, due to a similar basal meningitis, while it is not established that the implication of the ciliary ganglion is an essential part of the tabetic process. The pathology of the sympathetic involvement will be considered farther on in this paper.

The fact that Thomas,<sup>41</sup> in each of six cases, found decided changes in the spinal ganglion cells in no way invalidates the pathogenesis of Nageotte for "reaction à distance" is a well ascertained certainty. Besides, some of the cases of Redlich,<sup>42</sup> Marie and Leri<sup>43</sup> show distinct direct involvement of the spinal ganglia by an inflammatory process which has evidently extended from the meninges. This extension is not at all surprising when one remembers that even the purely mechanical lesions of the root described by Lejonne in cases of cerebral tumor sometimes reach the ganglia.

When the ganglion is directly affected by such an interstitial inflammation, it is not difficult to understand that the function of the cells becomes impaired, or even that their death may ensue. This will be manifested by a dentritic degeneration, which may well begin in the most distant parts, and hence give rise to the symptoms and postmortem appearance of the peripheral neuritis in tabes as described by Déjérine and others.

I do not, however, wish to exclude the primary peripheral origin of the nerve degeneration in some tabetics, for the infection at the root of tabes does not seem to be confined to the neural canal, as is shown by recent researches, which have shown the commonness of grave interstitial changes in the liver, spleen, and other viscera. Strong objection to the pathogenesis advocated in this paper has

<sup>38</sup> Neurol. Icon. Salpet., 1907; Gaz. des hôp., 1906, p. 687; 1906, p. 2.

<sup>39</sup> Soc. méd. des hôp. de Paris, November, 1901.

<sup>40</sup> Semeiology du système nerveux, Traité de Path. Gén. de Bouchard et Brissaud.

<sup>41</sup> Rev. neur., 1906, p. 573.

<sup>42</sup> Arbeiten aus dem Institut f. Anatomie und Physiologie, 1896, 985.

<sup>43</sup> Traité de Méd., Bouchard-Brissaud, 1904, ix.

recently been made by Beutler<sup>44</sup> on account of the very marked vascular engorgement he found developing in the posterior columns of 14 cases most carefully examined. He believes this too great to be accounted for by the meningitis always present. But it is not unusual to find vascular engorgement of neural tissue undergoing degeneration, and, as previously pointed out, the meningeal lesions tend all the time to regress and leave little trace. As pointed out by Paviot<sup>45</sup> they are often destroyed in the postmortem manipulation.

Spiller, in a verbal communication, states that he invariably finds meningitis present in cases of tabes when carefully examined.

**THE NATURE OF THE TABETIC PROCESS.**—The transitions between frank tabes, general paralysis, and cerebrospinal syphilis are shown by such cases as the six of Guillan and Tahon<sup>46</sup> and the two of Camp,<sup>47</sup> in which decided meningitis of the cord and vascular syphilitic lesions accompanied the tabetic process. It is unfortunate that in the case of the latter the radicular nerves were not examined. It must not be forgotten that Nageotte and Babinski contend for the primary meningeal location of the disease, and they believe the lymphocytosis to be sufficiently presumptive of this. Marie and Guillain,<sup>48</sup> although they suppose the affection to be purely syphilitic, think that some peculiarity of the lymph circulation in the posterior columns confines the disease to that region. They do not attempt to explain the lesions on the posterior root, for Guillain's<sup>49</sup> experiments only show that the lymph circulation is from the pia toward the central canal.

The experiments of Orr and Rows further show a circulation of lymph from peripheral nerve via spinal ganglion as well as anterior root, into meninges and cord in its whole circumference. These and other considerations led Ford Robertson and Macrae<sup>50</sup> to interpret the tabetic process as a specific one due to a toxin, non-syphilitic, originating in diphtheroid organisms situated in mucous membrane, and whose activity was rendered possible by the lowering of bodily resistance due to antecedent depressing conditions, of which syphilis is probably the commonest.

That meningeal reactions may be produced in this way is shown by Orr and Rows, but as Robertson and Macrae are making further experiments to answer the bacteriological objections made to their contentions, the consideration of this theory must be left to a future occasion.

<sup>44</sup> Thèse de Lyon, 1905.

<sup>45</sup> Soc. méd. des Hôp. de Lyon, 1905.

<sup>46</sup> Soc. Biol., January, 1905.

<sup>47</sup> The Difficulty of Diagnosis between Cerebrospinal Syphilis, Univ. Penna. Med. Bull., xviii, p. 167.

<sup>48</sup> Rev. neur., January, 1903.

<sup>49</sup> La circulation de la lymphe dans la moelle épinière, Rev. neur., December, 1899.

<sup>50</sup> Rev. Neur. and Psy., 1904; May, 1905; February, March, and April, 1906. The Pathology of General Paralysis, Brit. Med. Jour., 1905.

**THE SYPHILITIC NATURE OF THE PROCESS.**—When the nature of the tabetic process is considered, it is more difficult to steer a clear course. Each in its way, the researches of Marie and Guillain, of Nageotte, of Orr and Rows, and of Ford Robertson and Macrae tend to show that the affection is one of lymphatic distribution, but here agreement ceases. For Nageotte, it is tertiary syphilis of the meninges, and the toxic lymph attacks the nerve root where it makes most intimate and long contact, that is, at the point where it receives its meningeal sheath.

The directly syphilitic nature of the process is supported by such facts as those of Brissaud and Oberthur,<sup>51</sup> Dorlan,<sup>52</sup> and of Duhot,<sup>53</sup> who reported two cases ensuing respectively two and four years after infection. In each of these the process was rapidly and definitely arrested by intensive mercurial treatment. Another significant fact is reported by Dalous<sup>54</sup> as follows: Out of 21 tabetics presenting pathognomonic, tertiary lesions, 9 denied knowledge of infection or recollection of secondary symptoms.

**TABETIC SYMPTOMS IN SECONDARY SYPHILIS.**—Symptoms regarded as pathognomonic of tabes are found even in the secondary stage of syphilis. Buttino<sup>55</sup> examined 70 syphilitics from this point of view, mostly during the first year of the disease. He found in a large number of cases a diminution of a transient nature in the light reflex. In 16 cases he found an evanescent leukocytosis. Babinski<sup>56</sup> found it in 7 out of 74 syphilitics of long standing without any nervous symptoms. Dufour<sup>57</sup> examined 611 patients, and found it only in 7, all of whom confessed syphilis. Charpentier<sup>58</sup> failed to find the sign in 1100 healthy individuals, while Sulzer<sup>59</sup> found a fleeting Argyll-Robertson sign in 12 out of 50 syphilitics he examined from this point of view. Dupuy Dutemps<sup>60</sup> and Cestan's research established the fact, and Mantoux<sup>61</sup> collected 64 cases of this kind. Ravaut<sup>62</sup> and Belêtre found lymphocytoses in 58 out of 138 cases of secondary syphilis. This was often associated with exaggeration of the knee reflexes; and both conditions were recovered from under specific treatment. This exaggeration of the reflexes in no way modifies the point of view here sustained; for in polyneuritis, an exaggeration precedes a loss of the deep reflexes.

The association of lymphocytosis and reflex iridoplegia has been insisted upon by Babinski<sup>63</sup> and Nageotte, as has also the association

<sup>51</sup> Congrès de Lille, 1906.

<sup>52</sup> Thèse de Paris, 1906.

<sup>53</sup> Ann. de la Polyclin. Brux., 1903.

<sup>54</sup> Les lésions spécifiques dans le tabes, Rev. de Méd., 1904.

<sup>55</sup> Riv. di. Pat. Nerv. e. Ment., 1906.

<sup>56</sup> Rev. neur., 1898.

<sup>57</sup> Soc. méd. des hôp., 1902.

<sup>58</sup> Thèse de Paris, 1899.

<sup>59</sup> Ann. de dermat. et de syph., 1901, p. 239.

<sup>60</sup> Le signe pupillaire d'Argyll-Robertson. Sa valeur semeiologique, ses relations avec la syphilis, Gaz. des hôp. de Paris, December, 1901, xxviii.

<sup>61</sup> Thèse de Paris, 1904.

<sup>62</sup> Soc. méd. des hôp. de Paris, 1901.

<sup>63</sup> Rev. neur., 1901; Soc. méd. des hôp., 1901.

of the latter with aortitis, now known as the syndrome of Babinski. Irregularity of the pupil was found 12 times in 80 old syphilitics, 5 of them without tabetic symptoms.

**TABES NOT A TRUE SCLEROSIS.**—The postulate of Weigert that the disappearance of the noble elements is followed by neuroglia proliferation has probably been utilized excessively in the interpretation of such scleroses as are found in locomotor ataxia; for in a pure secondary degeneration of the noble element of the posterior columns due to the excessive pressure of the cerebrospinal fluid upon the posterior roots in cases of cerebral tumor, Lejonne found no neuroglia proliferation in the 15 cases examined. Leri<sup>64</sup> proved by measurement also that the apparent increase of connective tissue elements in the corpus callosum in senile degeneration of the brain was in reality due merely to their closer approximation, from the disappearance of the nerve structures proper. In some cases the corpus callosum was less than half the usual thickness. The diminution of volume in the posterior column in tabes is a pathological fact; and the sclerosis is therefore not hyperplastic but cicatricial. The same considerations apply to the wasting of the posterior roots found by Phillippe<sup>65</sup> in advanced cases of tabes. This absence of sclerosis during an inflammation generally regarded as interstitial has been recently remarkably exemplified by Raymond<sup>66</sup> in a case of comparatively acute multiple sclerosis.

**WHY THE SENSORY SYMPTOMS ARE IRREGULAR.**—Why then is there irregularity and seeming anomaly in the sensory manifestations of tabetics? Is it not evident that in a process so widespread and irregular in its distribution, it must necessarily be of unequal incidence upon different portions of the nerve roots. That local peculiarities will determine the inclusion of now one bundle, now another, is well shown in such chronic involvement as Pott's disease, in which the research of Fry<sup>67</sup> shows that the same process may pick out and moreover affect unequally, here a band of protopathic fibers, there a band of epicritic; for in his case of cervical Pott's disease, the patches of anesthesia were most irregularly distributed in location, degree, and modality. These may be bundles of epicritic or of protopathic fibers.

One must take into account, too, the errors induced by the exceeding crudeness of the usual clinical investigation of the sensibility, before the researches of Head had indicated methods of precision.

The declaration of changes, more particularly in thermic sensibilities, antedating Head's research, is of small relative value, unless the actual temperatures employed are noted; while the fallacies of the clinical methods in the investigation of touch are by this time

<sup>64</sup> *Le cerveau senile*; Congrès de Lille, 1906.

<sup>65</sup> *Arch. de neur.*, 1897.

<sup>67</sup> *Jour. of Nerv. and Ment. Dis.*, 1907, p. 185.

<sup>66</sup> *L'Encéphale*, 1907, p. 225.



familiar to every neurologist. The conclusions of the careful psychometric research of Vaschide,<sup>66</sup> the only one of which I am aware, are vitiated by these considerations.

The investigation of the tactile sense by the haphi-esthesiomètre of Toulouse-Vaschide<sup>66</sup> is in reality one of the sense of deformation; for its principle is the appreciation of weight. This appears in the research itself, of which one of the conclusions is that the trichesthesia is less involved in the tabetic process. Now Head has shown that the trichesthesia is a tactile function entirely dissociated from the deep sensibility. Vaschide's research, therefore, furnishes valuable data when interpreted in the light we have obtained from Head. In his investigation of temperature, of which the amounts are given, the distinction of epicritic fibers is very manifest with regard to certain roots.

It is possible that the vulnerability of fibers even depends upon the distinction which has been attempted between those of slender structure myelinating late and subserving the life of relation, passing up the cord by the zones of Lissauer (which, however, Nageotte believes to be endogenous); and thick ones early surrounded by myelin whose function is that of internal tactility, including the conscious notion of attitudes subserved by the telencephalon, and the automatic tonus regulating sense presided over by the cerebellum. Bonnién<sup>70</sup> declares that the vestibular nerve is the homologue of the latter posterior fibers, and that a predilection of tabes for this nerve as against the cochlear portion, homologous with the finer fibers, is thus accounted for. As Head has shown, it appears that a single peripheral fiber may convey an impulse which in the cord may select either of these paths.

Were these latter functions always attacked concomitantly, it would be a conclusive proof that the process originated outside the central nervous system; for these two functions follow different paths in the spinal cord, the impulses which go to the cerebrum reaching there homolaterally via the posterior columns, and heterolaterally via the lemniscus, the optic thalamus, and the internal capsule; while the cerebellum receives its information homolaterally via the lateral columns, the restiform body, and the peduncle, and also heterolaterally via Gower's tract and in the main the superior peduncle.

The situation of these cerebellar tracts at the periphery of the cord causes a suspicion that they may be peculiarly susceptible to toxin by extension from the meninges, and may play a greater part in the ataxia of tabetics than one is willing at present to admit;

<sup>66</sup> *Bul. ins. gen. psy. de Paris*, 1903, iii, No. 5.

<sup>67</sup> *L'Examin. des Sujets* (dans le Bibliothèque Internationale du Psychologie Expérimentale de Toulouse).

<sup>70</sup> *Le tabes labyrinthique*, Nouv. Icon. Salpet., 1899; *Le sens des attitudes*, Paris; *Le nerf labyrinthique*, Nouv. Icon. Salpet., 1904; *Le Vertige*, 1904.

although recent researches of Crouzon<sup>71</sup> and of Lejonne<sup>72</sup> show how often they are affected in the mixed scleroses of the aged. But clinical investigation has not yet ascertained whether these functions are in tabes always concomitantly effected. In the periphery, however, a single path appears to convey all impulses subserving sense of attitude whether these ultimately become conscious or not (Head).

**VESTIBULAR TABES.**—Pierre Bonnier lays great stress upon the vestibular causation of much of the ataxia as well as the oculomotor palsies of tabes. Though it cannot be said that his contention has been seriously examined by others in the light of careful clinical observation, yet it does not seem that clinical study, imperfect as it is, could have failed to distinguish between kinesthetic ataxia and that of vestibular origin. Nor is all disorientation of vestibular source.

This is proved even in the cephalic segment by the vertical stick illusion, in which, with eyes closed and head inclined, a grasped vertical rod appears to incline away from the side to which the head leans; and this phenomenon is quite unaffected by the condition of the semicircular canals or their nerves. It is probably due to kinesthetic interpretations coördinated by experience, and does not differ in the principle of its mechanism from such illusions as the up and down movements of the telegraph wires when passing them in the train, the appearance of the moon passing behind the clouds when in reality the clouds are crossing the moon, and from the deception of altitudes lent by distance, all these being due to the interpretation of unusual experiences by usual standards.

**TABETIC STRABISMUS AND NYSTAGMUS.**—Bonnier refers the oculomotor palsies to what he terms the bulbar syndrome provoked by irritation of the vestibular nerve, and irradiating via Deiter's nucleus toward one or more of the bulbopontine and mesencephalic nuclei from which Deiter's receives fibers, that is, those of the third, fourth, fifth, sixth, eighth, ninth, and tenth cranial nerves. He attributes to this mechanism the tinnitus, deafness, giddiness sudden falls, even without vertiginous sensations, which sometimes occur in tabetics, as well as Romberg's sign and the oculomotor palsies. He thinks that their basophobia is due to a similar overflow into the pneumogastric, producing a bulbar state corresponding to the emotion of terror, and due to what he terms an unconscious vertigo. He insists that we are no more conscious of the state of absence of vertigo than we are of the absence of thirst; and hence can describe its numerous ways of occurring in only vague terms.

The fact that a patient often falls without any consciousness of vertigo is attributed by Bonnier to the suddenness by which Deiter's

<sup>71</sup> Les scléroses combinées de la moelle, Thèse de Paris, 1904

<sup>72</sup> Arch. gén. de méd., 1905, p. 3009.

neucleus is stimulated by peripheral irritation of the great posterior root, the eighth nerve. He falls before a nerve impulse reaches the cerebrum and constitutes an impression in consciousness. He compares this fall to that of the epileptic without aura.

Etienne<sup>73</sup> has recently reported a similar case.

It remains to be seen whether these cases really differ from those described by Gowers<sup>74</sup> as vagal attacks, which often appear to be of true epileptic nature. They, however, differ in that consciousness is retained in the latter.

**THE OPTIC ATROPHY IS DUE TO BASAL MENINGITIS.**—The pathological evidences derived from the examination of the optic nerve in tabetics strongly confirm this view of the pathogenesis of the tabetic process.

Originating in the large ganglion cells of the retina, these fibers run a long course in close contact with the meninges until they reach their destination in the superior colliculus and the lateral geniculate body; and although they are not the homologues of posterior root fibers, but of the arcuate fibers in the medulla and the medial lemniscus in the midbrain, yet they are subjected on account of their situation to the same extension of inflammatory processes upon the meninges as are the posterior roots. Although it has been sustained by Popoff and Von Grosz<sup>75</sup> that the lesions were primitively retinal, on account of the disappearance of the ganglion cells of that membrane, yet the persistence of many cells there, even when the optic nerve is completely atrophied, has been shown by Marie and Leri.<sup>76</sup> This would seem to indicate that the process is not primitively ganglionic. It is right to say, however, that Dupuy-Dutemps<sup>77</sup> strongly contends that the real cause of the lost light reflex is a diseased condition of the nerves of the iris.

The amaurosis proceeding from the periphery, and the optic atrophy are the clinical concomitants of this peripheric invasion of the optic nerve. The rarity of the commencement of a tabetic amaurosis by a central scotoma is only to be expected when one recollects that the macular bundle runs in the centre of the optic nerve except at the very beginning of its course, where it is peripheral, upon the mesial side of the nerve (Henschen<sup>78</sup>). It is its involvement at this spot which accounts for the few cases of central scotoma of tabetic causation (Galezowski<sup>79</sup>).

The central scotoma which ensues upon a hemianopic contraction of the visual field has, however, a different significance; for this is due to the invasion of the macular bundle in the heart of

<sup>73</sup> Un cas de syndrome de Bonnier, *Rev. neur.*, 1907, p. 1025.

<sup>74</sup> Vagal Attacks, *Lancet*, June, 1907.

<sup>75</sup> *Congrès Internat. d'Ophthal.* Utrich, 1889.

<sup>76</sup> *Nouv. Icon. Salpet.*, 1904, p. 368.

<sup>77</sup> *Con. d'Ophthal. de Paris*, 1906; *Annals Oculist*, 1905.

<sup>78</sup> *Klinische und Anatomische Beiträge zur Path. des Gehirns*, Zweite Theil, Upsala, 1892.

<sup>79</sup> *Le fond de l'œil dans les affections du système nerveux*, Thèse de Paris, 1904.

the nerve in the course of an infiltration proceeding usually from the mesial side (R. Jocqs<sup>80</sup>) (Galezowski).

The very bad prognosis in these cases is due to the smallness of the macular bundle and the fact that a hemiopic contraction is a proof that this bundle has been reached by the inflammatory process. The bundle in the bandalette described by Marie and Leri,<sup>81</sup> which they have always found intact in common with that of Meynert<sup>82</sup> in cases even of complete optic atrophy, has nothing to do with the optic fibers, but runs between the sublenticular region and the basal optic ganglion of Meynert.

Nageotte believes that the zonula of Zinn is the usual site of the lesion.

THE SYMPATHETIC SYMPTOMS ALSO ARISE RADICULARLY.—It may appear strange that our point of view should be confirmed by those tabetic symptoms which are usually referred to the sympathetic nervous system. It will be recollected that Duchenne at one time thought that the lesions found in the cord and roots might be due to a hyperemia induced by a paralysis of the great sympathetic by the tabetic process, and a memorable controversy arose with Vulpian with regard to this. The latter, indeed, found sympathetic lesions only exceptionally, while Charcot,<sup>83</sup> in 1888, stated that even in subjects who had suffered for years from gastric crises, there was no change in the nerves and ganglion of the solar plexus. Raymond,<sup>84</sup> in 1894, thought the integrity of the sympathetic was demonstrated.

This was the state of matters when Jean Ch. Roux<sup>85</sup> was inspired in 1900 by Déjérine to investigate the question. He examined seven tabetics and ten subjects dead of other nervous and other diseases. In all the latter he found the sympathetic healthy, while in not one tabetic did he fail to find marked and identical modifications in the sympathetic chain and the great splanchnic.

In both of these and in all the cases he found that the small myelinated fibers were diminished in number, in the chain from 4400 to about 500, in the splanchnic from about 2000 to about 1150. It will be recollected that these myelinated fibers are derived from the spinal cord, certainly from the intermediolateral column, where Bruce<sup>86</sup> found as many as 8000 characteristic cells, and possibly from other regions of the gray matter. They are slender fibers possessing a myelin sheath. They leave the cord by the anterior and posterior roots; and they terminate around the sympathetic ganglion cells, from which another fiber takes up the nerve impulse

<sup>80</sup> Atrophie optic tabétique et scotome centrale, Extrait du Recueil d'Ophthalmologie, April, 1906.

<sup>81</sup> Rev. neur., 1905, p. 193.

<sup>82</sup> Leçons cliniques, 1888.

<sup>83</sup> Thèse de Paris, 1900.

<sup>84</sup> The Intermedio-Lateral Tract., Rev. neur. and Psy., 1907.

<sup>85</sup> Psychiatry, Trans. by Sachs, 1887.

<sup>86</sup> Leçons cliniques, 1894.

to terminate in muscle and gland. These latter are the so-called fibers of Remak, and possess no myelin sheath. Neither communicate with the posterior root ganglia.

Now, unless Roux's findings are due to an autonomous lesion, they must be secondary to a process in one or both of two regions, that is, the gray substance of the cord or the spinal roots; and as lesions of the gray substance of the cord have scarcely been observed in tabes, this degeneration of the myelinated sympathetic fibers must be due to the root lesions Nageotte has described. That this is the case Roux showed by observing their degeneration in cats after section of the spinal roots.

That this is not a general part of a peripheral neural degeneration was shown by the conservation of other peripheral nerves such as the intercostal. The sympathetic ganglia, too, were not diseased, nor are any changes presented by the large myelinated fibers which come from the spinal ganglia, as Roux shows these latter were intact in all the cases. Moreover, the diminution of slender myelinated fibers was proportional in the sympathetic to their decrease in the posterior roots in each case.

It is to the destruction of these that Roux attributes the anesthesia of the testicle, bladder, breasts, and trachea, as well as that of the stomach, which he has specially studied. The lack of the sensory innervation is for him the cause of the vesical hypotonia with its consequent ataxia, to which is due the micturitional difficulties of the tabetic. It is to a similar mechanism he attributes the gastric atony, which he believes responsible for much of the ill health and even of some of the gastric crises occurring in this disease.

Genouville<sup>87</sup> showed that when a tabetic bladder is touched by a sound a desire to urinate often follows, while this is not the case in normal persons. To a paresthesia of similar mechanism, Roux attributes the gastric crises and segmental referred pain which his observations show to be frequently provoked by dietetic errors or by drugs. The mechanism does not appear to me to differ in principle from that in a case I now have under observation, in which athetoid movements of the toes take place on stimulation of the skin even by exposure to cold.

The researches of Köster<sup>88</sup> into the trophic changes ensuing upon experimental section of the posterior roots show them to differ in no way from those in tabetics and thus confirm this hypothesis.

I may then conclude:

1. Tabes dorsalis is a secondary degeneration in the posterior columns, due to a chronic meningitis, very probably of syphilitic nature.

<sup>87</sup> Thèse de Paris, 1894.

<sup>88</sup> Zur. Phys. der Spinalganglion und der trophisch Nerv. and zur path. d. tabes; Leipzig, Engelmann, 1904.

2. The arrangement of the meninges surrounding the radicular nerve renders it peculiarly susceptible at that spot to mechanical or toxic injury.

3. The unequal incidence of the affection upon different fibers of the posterior root is probably due to unascertained peculiarity of structure or arrangement of fasciculi, rather than to any selective toxic influence.

4. The lesions tend toward resolution and arrest, even though the process may continue during the life of the individual.

5. With this arrest, regeneration tends to occur in the radicular nerve, the amount in the anterior root being relatively considerable while that in the posterior root is less in amount and functionally insignificant, as a rule.

6. The otherwise inexplicable vasomotor and cranial nerve symptoms and postmortem findings in this disease are shown thus to be necessary concomitants of the tabetic process.

7. The question of the pathogenesis of the polyneuritic manifestations found in tabetics is not yet answered.

The practical appreciation of the foregoing considerations to the treatment of tabetics need not be enlarged upon, as it does not come within the scope of the title of this paper; but when correctly applied, I believe another illustration will be afforded of the principle, *Naturam morborum curationes ostendunt*.

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## **A FURTHER CONTRIBUTION TO THE HERPETIC INFLAMMATIONS OF THE GENICULATE GANGLION.**

**A SYNDROME CHARACTERIZED BY HERPES ZOSTER OTICUS, FACIALIS, OR OCCIPITOCOLLARIS, WITH FACIAL PALSY AND AUDITORY SYMPTOMS.**

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THIS communication is a further elaboration of a syndrome presented at the American Neurological Association, in June, 1906.<sup>1</sup> At that time, three well-recognized clinical types of herpes zoster of the face and neck, with facial palsy and acoustic symptoms, were fused into a single group. The characteristic symptoms

<sup>1</sup> Herpetic Inflammations of the Geniculate Ganglion: A New Syndrome and its Complications, Trans. Amer. Neur. Assoc., 1906; Jour. of Nerv. and Ment. Dis., February, 1907; Archives of Otolaryngology, August, 1907.

were attributed to a specific, herpetic inflammation (*posterior poliomyelitis*) of the geniculate ganglion of the facial nerve; and the neural complications, to an extension of the inflammatory process to the adjacent seventh and eighth nerves (Fig. 1). The zoster zone for the geniculate ganglion was thought to be intercalated between the zones of the Gasserian in front and the cervical ganglia behind, and situated on the tympanum, auditory canal, and interior parts of the auricle.

The distinctive features of the clinical picture are as follows: Herpes facialis, herpes oticus, or herpes occipitocollaris, with facial palsy; and in some of the cases irritative and paralytic symptoms referable to the acoustic nerve.

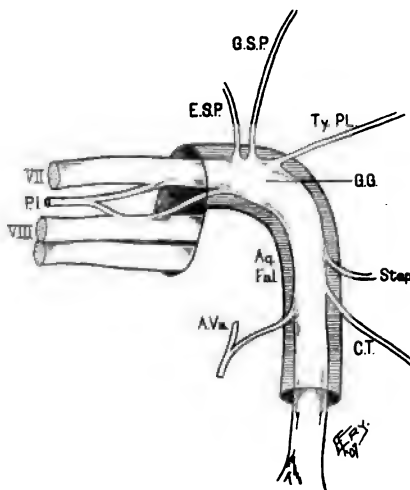


FIG. 1.—The geniculate ganglion, its relations to the facial and auditory nerves: VII, facial nerve; P.I., pars intermedia; VIII, auditory nerve; Aq.Fal., aqueduct of Fallopius; G.G., geniculate ganglion; E.S.P., external superficial petrosal; G.S.P., great superficial petrosal; Ty.PL., branch to the tympanic plexus. (Cunningham's Anatomy.)

The subject matter of the paper may be conveniently considered under the following headings:

I. The syndrome and its clinical types.

A. Herpes oticus.

B. Herpes oticus, with facial palsy.

C. Herpes oticus, with facial palsy and hypo-acousis.

D. Herpes oticus, with facial palsy and Ménière's complex.

II. Sub-groups of the syndrome.

Herpes facialis, with facial palsy and auditory symptoms.

Herpes occipitocollaris, with facial palsy and acoustic symptoms.

Herpes zoster of the cephalic extremity, with auditory nerve complications.

- III. Multiple involvement of ganglia in herpes zoster.
- IV. The cranial nerve ganglia and their relation to herpes zoster.
- V. The zoster zone of the geniculate ganglion.
- VI. Sensory symptoms in the trigeminal and cervical zones in herpes zoster oticus.
- VII. The ganglia of the glossopharyngeal and vagus nerves and their probable role in zona.
- VIII. Concluding remarks.

I. THE SYNDROME AND ITS CLINICAL TYPES. *Group A. Herpes Oticus.* This, the simplest expression of the affection, is dependent upon an herpetic inflammation (*posterior poliomyelitis*) of the geniculate ganglion. It may be preceded by the mild prodromal symptoms of herpes zoster, with preherpetic pains localized in the ear and mastoid region (otalgia). The eruption, which varies considerably in extent, is distributed over the tympanum, external auditory canal, concha, tragus, antitragus, helix, antihelix, and occasionally overlaps into an adjacent marginal zone. In this cone-shaped area is the ganglionic representation and zoster zone of the geniculate ganglion.

In some cases the auricle may be considerably swollen, red, and tender, standing out somewhat from the side of the head. Often the meatus and canal are so reduced in size as to render the introduction of a speculum difficult and painful. Naturally, when the conduction mechanism of the external ear is infiltrated and swollen tinnitus and some temporary deafness may result. This must be carefully distinguished from neural deafness, which will be described in other groups of the affection. The inflammatory swelling subsides rapidly, the eruption desiccating and disappearing in about a fortnight. Postherpeticotalgia, in some cases, may persist for a considerable time.

*Group B. Herpes Oticus, with Facial Palsy.* In addition to herpes oticus there is an associated peripheral facial palsy on the corresponding side. The paralysis is complete, involving all branches of the nerve, making its appearance with or soon after the eruption becomes manifest. All degrees of severity have been observed, from a very transient form, lasting only a few days, to that which leaves a permanent weakness and contracture. In this group the adjacent facial nerve has been involved in the inflammatory process.

*Group C. Herpes Oticus, with Facial Palsy and Hypo-acousis.* In this group, with herpes oticus and facial palsy, there is an associated disturbance of hearing. This consists of a diminution of the acuity of audition with or without tinnitus aurium, and is a milder type of acoustic disturbance. It may be quite transient. It is to be ascribed to an extension of inflammatory products to the auditory nerve which is close by.



*Group D. Herpes Oticus with Facial Palsy and Ménière's Complex.* This is a very severe manifestation and has associated with the foregoing symptoms all the characteristics of Ménière's syndrome: tinnitus aurium, deafness, vertigo, nystagmus, vomiting, and disturbances of the equilibrium.

This group may also be explained by the extension of inflammatory products along the nerve sheaths to the terminations of the auditory nerve. (It is in my opinion very probable that the *ganglia* of the auditory nerve may be primarily involved in the specific inflammations of *zona*.)

REMARKS. The four groups of cases just outlined are all dependent upon specific herpetic inflammations of the geniculate ganglion, representing different degrees of severity. The eruption is confined to the geniculate ganglion zone; the other zoster zones of head and neck are free. The neural complications result from the proximity of the inflamed ganglion to the seventh and eighth nerves.

II. SUB-GROUPS OF THE SYNDROME. *Herpes Facialis with Facial Palsy and Acoustic Symptoms.* In this clinical type the eruption makes its appearance upon the face, an area represented by the Gasserian ganglion; the zoster zone of the geniculate is free. Facial palsy may be the sole neural complication, as in herpes oticus (Group B), or there may be associated disturbances of the auditory nerve.

*Herpes Occipitocollaris, with Facial Palsy and Acoustic Symptoms.* The herpetic eruption in this group is distributed over the occiput, the side of the neck, the inner surface and the posterior half of the outer surface of the auricle, and a patch corresponding to the angle of the jaw (herpes occipitocollaris). This skin area represents the zoster zones for the second, third, and fourth cervical ganglia. The zones for the geniculate and Gasserian ganglia are free. The neural complications do not differ from those described in the previous group.

*Herpes Zoster of the Cephalic Extremity, with Auditory Complications.* The occurrence of auditory complications in connection with herpes facialis, occipitocollaris, and herpes oticus, have already been mentioned. With the auditory symptoms there has been associated a peripheral facial paralysis. In my first paper this involvement of the auditory nerve was ascribed to an extension of the inflammatory process from the geniculate to the auditory nerve and its terminations, the envelopment of the facial, the nerve of Wrisberg, and the acoustic in a common sheath in the depths of the internal auditory canal favoring such an extension.

The great severity, however, of the acoustic disturbances in some of these cases, and their persistence, has suggested the thought that the acoustic ganglia themselves may be the seat of a primary inflammatory involvement (Fig. 2). It will be recalled that the cells of the ganglion of Scarpa and ganglion of Corti take their origin

from the neural ridge, an embryonic structure from which the other ganglia liable to zoster are derived. Clinical confirmation of this theory is found in the occurrence of acoustic symptoms in herpes zoster of the face, without an associated facial paralysis. In cases of this type, if the acoustic nerve were involved by reason of its proximity to the geniculate ganglion, the facial nerve could hardly escape a simultaneous involvement.

The following cases show that auditory symptoms may accompany herpes facialis and herpes oticus, without a corresponding facial palsy:

Casse.<sup>2</sup> Observation I. A typical herpes zoster of the third division of the fifth nerve, in a woman, aged fifty-eight years. Accompanying these manifestations in the trigeminal distribution,

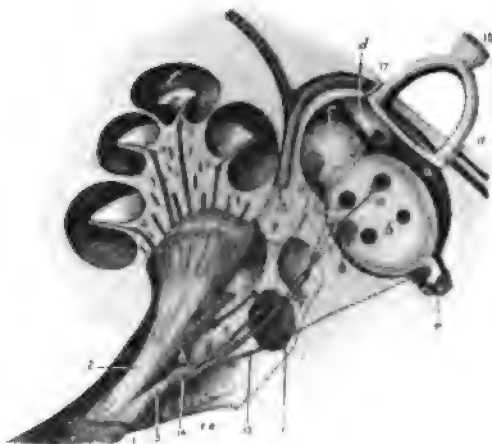


FIG. 2.—The ganglia and terminations of the auditory nerve: 1, auditory nerve; 2, cochlear branch; 3, vestibular branch; 4, ganglion of Corti; 6, ganglion of Boettcher; 14, ganglion of Scarpa; 15, facial nerve. (Testut's Anatomy.)

there were pains in the auditory canal, *roaring in the ear*, and *diminution of hearing*. The face was not paralyzed. Two months later there was still tinnitus aurium and slight diminution of hearing. The examinations of the ear, throat, and nose were negative.

Burin-Desrozieres.<sup>3</sup> Observation II. A man, aged thirty-one years. Exposure to cold October 7, 1904, followed by neuralgic pain in the right side of the face; on October 14 an eruption of herpes zoster developed on the right side of the face. On October 18 the neuralgic pain had practically disappeared, but there persisted a certain "*hardness of hearing*" on the right side. Facial palsy was not observed.

<sup>2</sup> Zona de la troisième branche du trijumeau, Thèse de Paris, 1902.

<sup>3</sup> Ibid., 1904.

Gruber,<sup>4</sup> in recording two cases of herpes zoster, limited to the external auditory canal (herpes oticus), states: "In both cases there was hardness of hearing and tinnitus, which was out of proportion to the lesion in the external auditory canal. It would seem as if, in these cases, the auditory nerve was involved perhaps reflexly. The opening of the vesicles did not relieve the hearing, which only returned with the disappearance of the other symptoms."

It seems to me, therefore, very probable that the acoustic ganglia may be primarily involved in the specific inflammation of posterior poliomyelitis.

**REMARKS.** In the chief group of the syndrome, it will be observed that the eruption is situated in the geniculate area (herpes oticus). In the sub-group it is distributed, either in the zone of the Gasserian ganglion (herpes facialis), or in the zones of the upper cervical ganglia (herpes occipitocollaris). In all, the neural complications, if present, are identical in sequence and symptomatology. I would also emphasize the group with herpetic eruption and auditory symptoms, without facial palsy. These cases may depend upon a primary involvement of the ganglia of the acoustic nerve, as it would seem very improbable that an inflammation could extend from the geniculate to the auditory nerve, without at the same time compromising the facial. The possibility of slight or transient facial palsies escaping observation, must, however, be kept in mind.

In my previous paper I collected 60 cases of herpes zoster of the cephalic extremity, with facial palsy; in 19 of these cases auditory complications were also present. The eruption in this series of cases had the following distribution:

	Cases.
Herpes oticus . . . . .	12
Herpes facialis . . . . .	12
Herpes occipitocollaris . . . . .	32
Herpes oticus and occipitocollaris (combined) . . . . .	3
Herpes facialis and occipitocollaris (combined) . . . . .	1

I would here remark that in the literature I found no recorded case of facial palsy and acoustic disturbance, complicating herpes zoster, in which the eruption was not situated on the cephalic extremity of the body. The question as to the occurrence of neural complications in herpes facialis and herpes occipitocollaris, the zoster zone for the geniculate being free from any eruption, I will consider under the next heading.

**III. MULTIPLE INVOLVEMENT OF THE GANGLIA IN ZONA.** Herpes zoster is an acute, specific, infectious disease, characterized by an inflammatory reaction in ganglia containing the so-called *spinal* or *unipolar type* of cells. Ganglia of this type are the spinal ganglia of the posterior roots, the Gasserian and geniculate ganglia of the

<sup>4</sup> Herpes Auricularis, Monatsch. f. Ohrenheilk., 1875, Nr. 5.

cranial nerves. The localization of a specific inflammatory process in the ganglia of the *spinal type* was termed Posterior Poliomyelitis by Head and Campbell, and the similarity of the pathological changes to those occurring in anterior poliomyelitis was pointed out. The fact was also emphasized that the essential pathological lesion is generally limited to a single ganglion, which corresponds to the eruption of zoster.

That more than one ganglion may be involved is shown clinically by the occurrence of double, triple, bilateral, and alternate forms of zona, the eruption appearing in more than one zoster zone. This tendency to involvement of more than one ganglion is especially frequent about the head and neck. I would call special attention to the fact that clinical evidence exists showing that some ganglia may be implicated in zona, without the occurrence of an eruption in their respective zones.

Symptoms indicating such involvement are to be found in the neuralgic pains and mild sensory disturbances (*hypalgesia* and *hypesthesia*) occasionally observed in zones adjacent to the chief or eruptive focus.<sup>5 6</sup> It is also possible that the so-called vesicles aberrantes<sup>7</sup> may be regarded in the same light. In zona the ganglion which corresponds to the eruption is to be regarded as the chief or *eruptive focus*. The inflammatory reaction is not confined solely to this ganglion, but inflammatory changes of a milder grade may also be present in adjacent ganglia, above and below. In other words, there may be a serial involvement of ganglia, the extent and intensity of which depends upon the severity of the infection. Such a theory of inflammatory reaction in a chain of ganglia, which shades off from the chief or eruptive focus, is also more in harmony with the acute, specific, toxic nature of herpes zoster, and the analogy which it bears to the anterior poliomyelitis, the chief or eruptive focus of the one corresponding to the permanent paralytic focus of the other, while the transient and mild sensory manifestations of herpes are the sensory equivalent of mild and transient palsies. I attach a special importance to this inflammatory involvement of a series of ganglia, in the relation which it bears to the sub-groups of the syndrome—the *herpes facialis* and *herpes occipitocollaris* with neural complications.

The Gasserian, geniculate, and upper cervical ganglia may be regarded anatomically as representing a more or less continuous ganglionic chain. Hence, if the chief inflammatory or eruptive focus were situated in any one, a milder, non-eruptive, inflammatory reaction might occur in other ganglia of the group. In herpes zoster of the face, with neural complications, the chief or eruptive focus is

<sup>5</sup> Champion, *Manifestation à distance dans la Zona*, Thèse de Paris, 1900.

<sup>6</sup> Weisenburg, *Herpetic Inflammation of the Cervical and Thoracic Nerves*, Jour. Nerv. and Ment. Dis., 1907, p. 726.

<sup>7</sup> Tenneson, *Vesicules aberrantes du zona*, Bull. de la Soc. méd. des hôp., 1898.

situated in the Gasserian ganglion; there has, however, been a coincident inflammatory reaction in the geniculate, sufficient to disturb the function of the adjacent nerves, without producing an eruption in the geniculate area. In the same manner, I would explain those cases in which, with neural complications, the eruption is confined to the zones of the second, third, and fourth cervical ganglia.

The neural complications (seventh and eighth nerves) observed in herpes zoster of the cephalic extremity may, therefore, be regarded pathologically as depending upon an herpetic inflammation of the geniculate ganglion.

*Pathological Evidences of Multiple Involvement of Ganglia.* The elaborate pathological researches of Head and Campbell<sup>a</sup> are now so well known that I will consider this phase of the subject only in its relation to multiple or serial involvement of ganglia; and its bearing upon the existence of lesions of slight degree in ganglia near the chief or eruptive focus.

Histological studies in cases of zona show that the ganglion corresponding to the eruption is the seat of well-marked inflammation and hemorrhages. In the acute stage the ganglion is swollen and cedematous, and is the seat of extensive round-cell infiltration and hemorrhages; the cells are in various stages of degeneration; later, as the inflammation subsides, there is connective tissue proliferation, and in severe cases a permanent scar results. In both acute and chronic stages secondary changes are demonstrable in the corresponding posterior root, as well as in the peripheral nerves.

I will here briefly analyze the pathological evidence existing at the present time of serial ganglion involvement, which, in my opinion, furnishes a pathological basis for the mild sensory symptoms already mentioned as manifesting themselves in the adjacent non-eruptive zones.

In order to demonstrate the presence of a mild inflammatory reaction in ganglia adjacent to the chief or eruptive focus, quite recent cases would be the most favorable, if not essential. In the event of the process being older, such changes would be more readily demonstrable in the posterior roots than in the ganglia themselves.

In the descriptions of Head and Campbell it would appear that the inflammatory changes in zoster are limited to a single ganglion—that which corresponds to the eruption. Essentially this is true, although the presence of milder changes, if present, should receive due weight. Their statement as to multiple involvement is as follows: "It is probable that two ganglia are occasionally affected together. From clinical observation, this seems particularly liable to occur with the second, third, and fourth cervical. Unfortu-

<sup>a</sup> Pathology of Herpes Zoster, Brain, 1905.

nately, no such case is included in our series of postmortem examinations."

It will be observed, however, from the following abstracts of some of their observations, that mild pathological changes were noted in ganglia adjacent to the eruptive focus and yet apparently having no corresponding zoster manifestations.

CASE I.—Herpes zoster in first lumbar distribution of left side; three days duration. Left first lumbar ganglion—typical inflammatory changes present. Right first lumbar—*the cells do not stain well.* Left and right twelfth dorsal ganglia—*bloodvessels are much engorged.* Left and right second lumbar ganglia—neither show any marked change.

CASE IV.—Herpes zoster in twelfth dorsal distribution of right side; three days duration. Right twelfth dorsal ganglion—typical inflammatory changes present. Left twelfth dorsal—right and left eleventh dorsal were free from *noteworthy* alterations.

CASE V.—Herpes zoster, eleventh dorsal distribution of left side; fourteen days duration. Left eleventh dorsal ganglion—typical inflammatory changes were present; the remaining ganglia were normal. There were marked secondary degenerations in the posterior root of the eleventh dorsal on the left side. *A few definitely degenerated fibers were seen in the left twelfth dorsal root.*

CASE VI.—Herpes zoster in left third cervical distribution; fifty-seven days duration. In left third cervical ganglion and left third cervical posterior root the typical changes were present. *Some bundles of the fourth root on the left side also seemed to have undergone change, but this was a less certain change than that of the third root.*

CASE VII.—Herpes zoster in left second dorsal region; ninety-six days duration. Typical changes in left second dorsal ganglion and posterior root. *In first dorsal root a few degenerated fibers could be recognized.*

It will thus be seen that in Cases V, VI, and VII there were distinct, although slight, evidences of ganglionic changes, indicated by degenerations in the posterior root.

Pathological observations published since the appearance of their work are even more convincing. Ballet,<sup>9</sup> in a case of herpes zoster occipitocervicalis of three weeks' duration, reports as follows: "The ganglia were not examined; marked degenerations are present in the third cervical posterior root. In the second cervical root it is with difficulty that degenerations are found, although they are distinctly present."

Armand-Delille and Camus,<sup>10</sup> in a case of herpes occipitocollaris of one month's duration, found marked chromatolysis in the cells

<sup>9</sup> *Lesions nerveuses dans un cas de zona cervicale*, Soc. des hôp., 1900, p. 706.

<sup>10</sup> *Soc. de neur. de Paris*, February, 1903.

of the left third cervical ganglion. Similar cellular degenerations were also present in the left second cervical ganglia, but less marked. There were corresponding degenerations in the second and third posterior roots. (This case is of especial interest pathologically, in that the ganglionic lesion was a cellular degeneration without the massive inflammatory reactions usually found.)

In a personal observation of herpes occipitocollaris with facial palsy—autopsy eighty-seven days after the appearance of the eruption—there were found well-marked degenerative changes not only in the third cervical posterior root, but also in the posterior root of the geniculate ganglion, the *pars intermedia* of Wrisberg.<sup>11</sup>

A most interesting observation is that of Hedinger.<sup>12</sup> A herpes zoster in the eleventh dorsal distribution of the left side; death occurred nineteen days after the appearance of the eruption. There was typical hemorrhagic inflammation in the left eleventh dorsal ganglion; in the left tenth and left twelfth dorsal ganglia similar changes are present, but much less severe. All the lumbar ganglia on the left side showed lymphocytic infiltration, diminishing in intensity downward, but especially well marked in the last lumbar. In the right lumbar ganglia only slight and insignificant changes were present. Similar changes were present and somewhat more marked in the right eleventh and twelfth dorsal ganglia.

In this case there seems to be no doubt as to the effect of the specific toxin of herpes zoster on a series of ganglia, although the eruptive manifestations were limited to the eleventh dorsal zoster zone. It will thus be apparent, from the more recent pathological studies of herpes zoster, that the inflammatory reaction in the ganglia is not so limited in its extent as a study of the eruption phenomena alone might lead us to infer, in this respect confirming the clinical observation of mild sensory disturbances—neuralgic pains, hypalgesia, hypesthesia—in zones free from the eruption, and also explaining the occurrence of facial palsy in herpes zoster of the face and neck, in which the geniculate zone is free from eruption.

IV. THE CRANIAL NERVE GANGLIA AND THEIR RELATION TO HERPES ZOSTER. I will now mention, briefly, certain facts relating to the anatomy and histology of the cranial nerve ganglia, and the probable role which these structures play in herpes zoster.

At the time of the presentation of my paper, June, 1906, the only recognized cranial nerve localization of zoster was that of the Gasserian ganglion, an inflammation of this ganglion giving rise to the well-known herpes facialis, concerning which, an abundant literature has grown up. Barnes,<sup>13</sup> however, in 1903, in the report of a case of herpes of the neck associated with facial palsy, made the following statement: "Hence this association of symptoms

<sup>11</sup> Jour. of Nerv. and Ment. Dis., February, 1907.

<sup>12</sup> Deut. Zeit. f. Nervenheilk., Band xxiv, S. 305.

<sup>13</sup> Trans. Clin. Soc., 1903, vol. xxxvi.

strongly suggests that the patient is suffering from the effects of an inflammation of three ganglia—one motor (the geniculate of the facial nerve) and two sensory (the third and fourth right cervical root ganglia)."

Vail<sup>14</sup> also, in his paper on herpes zoster auris, mentions the otic ganglion as a possible localization, in the following words: "Politzer and others have observed facial paralysis on the affected side. This would seem to indicate involvement of the otic ganglion, which I believe has a branch of the facial entering it."

The otic ganglion, or ganglion of Arnold, is not regarded by histologists as belonging to the spinal type. It is grouped with the sympathetic system of ganglia, in which the cell type is multipolar, and not unipolar. Therefore, according to the present pathological conceptions of the disease, it should be excluded from the realm of herpes zoster.

As regards the geniculate ganglion, it must be emphasized that this structure is not *motor*; histologically it belongs to the sensory ganglia, composed of the *unipolar* type of cells, and is, therefore, the homologue of the spinal and Gasserian ganglia. With its afferent fibers, the pars intermedia of Wrisberg, and its efferent fibers, the petrosal nerves, it forms the sensory system of the facial nerve. In other words, we have here a ganglionic structure manifesting the same susceptibility to zona as the Gasserian and spinal ganglia.

If the Gasserian and geniculate ganglia, by virtue of the unipolar cell type, belong to that series of ganglia liable to the inflammation of zona, the same would also be true of the ganglia of the glossopharyngeal nerve (ganglion of Andersch and ganglion of Ehrenritter) and of the vagus nerve (ganglion jugulare and ganglion plexiforme). These ganglia are also regarded by histologists as belonging to the *unipolar* or *spinal type*, and therefore cannot be excluded from the realm of herpes zoster.

I would also lay especial emphasis upon the possible role played by the ganglia of the acoustic nerve in this affection. All the posterior spinal ganglia, as well as the ganglia of the fifth, seventh (geniculate), ninth, and tenth cranial nerves, are developed from outgrowths of the embryonic structure known as the neural ridge. These ganglia are all of the so-called unipolar or spinal type. The ganglion of the acoustic nerve (ganglion acousticum) is also an outgrowth of the neural ridge, later becoming differentiated into the ganglion spirale of the cochlear nerve and the ganglion of Scarpa of the vestibular nerve. The cells of the acoustic ganglia are not, however, unipolar, but retain the primitive bipolar character (in fishes the cells of the spinal ganglia are bipolar, and it is only in higher types that the unipolar cells are found).

<sup>14</sup> Laryngology and Rhinology, 1906.



While the ganglia of the auditory nerve retain their bipolar character, their original source is the neural ridge, and it would appear very probable that they, as well as the other ganglia taking their origin from this structure, may be liable to the specific action of the toxin of zoster. This theory is confirmed clinically by the occurrence of very severe auditory nerve symptoms in zona of the face, ear, and neck. From the developmental and histological standpoint, I believe that we are justified in receiving the ganglia of the glossopharyngeal, vagus, and acoustic nerves into the realm of herpes zoster.

V. THE ZOSTER ZONE FOR THE GENICULATE GANGLION (HERPES OTICUS). In order to determine the exact extent and boundary of this zoster zone, accurate clinical observations in the future will be necessary—observations in which the whole extent of the eruption has been carefully noted and indicated on the various anatomical landmarks of the ear. There are, however, at the present time a sufficient number of accurately recorded cases of herpes oticus, by means of which a fair idea of the extent and probable boundaries of this zone may be determined, and which may serve as a basis for future investigations. The difficulties encountered in the interpretation of this area are considerably increased by the very complex innervation of the parts and the tendency to variation and overlapping of the zoster zones on the extremities of the body. It will also be recalled that the zones of the Gasserian and cervical ganglia are partially represented on the auricle, the herpes occipitocollaris encroaching on the auricle posteriorly, and the herpes facialis anteriorly. The zone for the geniculate is intercalated between these two areas. For the purpose of determining this zone, I have analyzed and tabulated seventeen cases of primary isolated herpes zoster oticus. It is, however, only the area in which the eruption is distributed to which I will call attention. This distribution corresponds in extent to the following anatomical landmarks: The tympanic membrane, the external auditory canal and meatus, the concha, tragus, antitragus, lobe of the ear (external surface), anthelix, and the fossa of the anthelix.

We may, therefore, assume that the geniculate ganglion is represented in an irregularly cone-shaped area, the apex corresponding to the tympanic membrane, the base situated on the external surface of the auricle. I do not believe that this entire area is represented by the geniculate ganglion alone. Allowance must be made for the overlapping of the Gasserian in front, and the cervical nerves behind. It is in my opinion, also, not improbable that future investigations will show that the ganglia of the glossopharyngeal and vagus nerves are also partially represented in this area.

	THE DISTRIBUTION OF THE ERUPTION ON THE ANATOMICAL LANDMARKS OF THE EAR BY X.											
CASES OF HERPES OTICUS.	Auricle.	Antihelix.	Fossa of helix.	Lobe.	Tragus.	Antitragus.	Concha.	External meatus.	External auditory canal.	Anterior wall.	Posterior wall.	Tympanum.
1. Berger, Neur. Central, 1905	X	..	..	..	..	..	..	..	X	..	..	..
2. Chavanne (Bilateral case). <i>Right</i>	..	X	..	..	..	X	X	..	..	..	..	..
3. Ann. Mal. de L'Oreille, 1906. <i>Left</i>	..	..	..	..	..	X	..	X	..	..	..	..
4. Gruber, Case 1	..	..	..	..	..	..	..	..	..	X	..	..
5. Monatschr. f. Ohrenheil., 1875. Case 2	..	..	..	..	..	..	..	X	..	..	X	..
6. Gruber, Zeitsch. f. Ohrenheil., vol. xlv	..	X	..	..	..	..	X	..	..	..	..	..
7. Hasslauer, Deut. Mil. Aerst. Zeit., 1905	X	..	..	..	X	..	..	..	X	..	..	..
8. Hammerschlag, Arch. f. Ohrenheil., 1901	..	..	X	X	X	..	..	..	..	..	..	..
9. Hammerschlag, Arch. f. Ohrenheil., 1898	..	..	X	X	X	..	..	..	..	..	..	..
10. Sommers, Amer. Med. and Surg. Bull., 1896	..	..	..	..	..	..	..	X	X	..	..	..
11. Serai. Zeit. f. Ohrenheil., vol. xlv	..	..	..	..	..	..	..	..	X	..	..	..
12. Szenes, Inter. Central. f. Ohrenheil., 1902	..	..	..	..	..	..	X	..	..	..	..	..
13. Tomka, Arch. f. Ohrenheil., 1900	X	..	..	..	..	..	..	..	..	..	..	X
14. J. R. Hunt, Jour. Nerv. and Ment. Dis., 1907	..	..	..	..	..	..	X	X	..	..	..	..
15. Personal Observation	..	X	..	..	..	..	X	X	..	..	..	X
16. Personal Observation	..	..	..	X	X	X	X	X	..	..	..	X
17. Personal Observation	..	..	..	..	X	..	X	X	..	..	..	..

VI. SENSORY SYMPTOMS IN THE TRIGEMINAL AND CERVICAL ZONES IN HERPES ZOSTER OTICUS. In some cases of herpes zoster oticus, symptoms referable to the trigeminal distribution have been noted. Tearing and shooting pains in one or more of the three divisions of the fifth nerve are mentioned (Hasslauer,<sup>15</sup> Anstie,<sup>16</sup> Hammerschlag<sup>17</sup>). The points of exit of the trigeminus were found tender on pressure (Berger<sup>18</sup> and Hammerschlag). Diminution or absence of the corneal and conjunctival reflexes (Berger, Hammerschlag, Ramsay Hunt<sup>19</sup>), hypesthesia and hypalgnesia of the face on the affected side have been observed. These fifth nerve symptoms are sensory in nature, and unaccompanied by a corresponding eruption of herpes.

I find an explanation for their presence in a mild inflammatory reaction of the Gasserian ganglion, but not of sufficient severity to produce the eruption. It must be admitted, however, that the neural connection between the geniculate ganglion and the second and third divisions of the fifth nerve (great and small superficial petrosal nerves) may give rise to a referred pain.

Mild sensory symptoms of a similar nature may, likewise, be

<sup>15</sup> *Deut. Mil.-Aerst. Zeit.*, 1905, vol. xxxv.

<sup>17</sup> *Arch. f. Ohrenheil.*, 1901, s. 16; 1898, s. 1.

<sup>18</sup> *Jour. of Nerv. and Ment. Dis.*, 1907.

<sup>16</sup> *The Practitioner*, 1871, p. 198.

<sup>19</sup> *Neur. Centralblatt*, 1905, s. 844.

present in the distribution of the cervical nerves in cases of herpes oticus. In one of my cases a typical example of herpetic inflammation of the geniculate ganglion, with herpes zoster oticus, facial palsy, and deafness, severe lancinations were present in the occipital region and neck for several days. In addition there were distinct hypalgnesia and hypesthesia on the left side of the face, head, and neck for two weeks. This sensory disturbance was not present below the level of the neck, and there were no stigmata of hysteria.

VII. THE GANGLIA OF THE GLOSSOPHARYNGEAL AND VAGUS NERVES AND THEIR PROBABLE ROLE IN ZOSTER. These ganglia, composed of unipolar cells, taking their origin from the neural ridge,

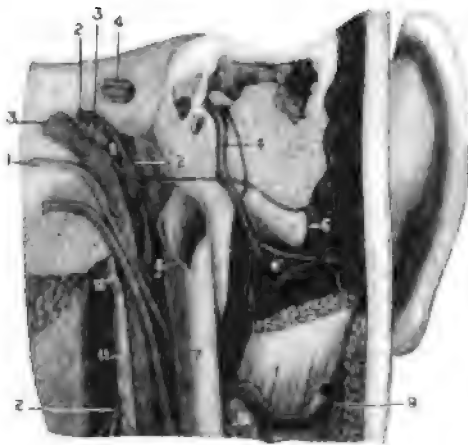


FIG. 3.—The ganglia of the ninth and tenth nerves, and the auricular branch of the vagus: 1, spinal accessory nerve; 2, glossopharyngeal; 2', ganglion of Andersch; 3, vagus nerve; 3', ganglion jugulare; 4, facial; 4', auricular branch of facial; 5, auricular branch of vagus; 6, anastomosis between the auricular branches of the facial and vagus nerves. (Testut's Anatomy.)

are the homologues of the posterior spinal ganglia (Fig. 3). Theoretically there is no reason why they should not be involved in cases of posterior poliomyelitis. From our knowledge gained by the dissection method alone, the ganglia of the vagus presumably have a skin representation on the posterior wall of the auditory canal, the posterior portion of the tympanic membrane, concha, and posteromesial surface of the auricle (*auricular branch of the vagus*). The glossopharyngeal ganglia through their communications with the vagus and facial nerves may also be represented in the same area. In an analysis of many cases of zona of the cephalic extremity, I have had constantly in mind the possibility of symptoms which might be ascribed to a disturbance of the vagus function. The following case, reported by Buys<sup>20</sup> is the only one coming under my notice, which might bear this interpretation:

<sup>20</sup> Bull. de la Soc. Belge d'otol., de laryng. et de rhin., 1898. Eruption herpétique du pavillon précédé de phénomènes nerveux considérables.

"A girl, aged seventeen years. Onset with headache and vomiting. Severe headaches continued with *stiffness of the neck*, and *frequent vomiting*. Photophobia, no fever or delirium. *The pulse was slow and irregular*. On the fourth day, the acuteness of the pain subsided and settled in the mastoid region of the right side. The mastoid was tender, as was the canal on the introduction of the otoscope. Hearing was diminished. On the fifth day herpetic vesicles made their appearance on the antitragus and lobule of the ear. The headache and neck pains are less severe. On the sixth day a fresh crop of vesicles made their appearance on the mesial surface of the pinna and the lobule. All pain disappeared in the course of a few days, and the hearing was restored. In fifteen days, the eruption had vanished."

The frequent vomiting and the slow irregular pulse in this case are strongly suggestive of a vagus disturbance. I would also emphasize the area of distribution of the eruption corresponding to the cutaneous filaments of the vagus. It will also be observed, in this case, that the hearing was affected, without any associated evidences of facial palsy, also suggesting a primary involvement of the acoustic ganglia.<sup>20</sup>

VIII. CONCLUDING REMARKS. The fusion of these clinical types into a single large group, with a common pathological basis, constitutes a well-defined clinical entity. It may be summarized as follows: A peripheral facial palsy complicating an eruption of herpes zoster on the cephalic extremity of the body. The eruption may be limited to the face, the head and neck, or the ear, or combinations of these (*herpes facialis*, *herpes occipitocollaris*, *herpes oticus*). The term herpes oticus I would confine to that group of cases in which the eruption is restricted to the cone-shaped zoster zone of the geniculate ganglion (the tympanum, auditory canal, concha, and an adjacent marginal area on the external surface of the auricle). With the facial palsy there may be associated symptoms referable to the auditory nerve. These are of two types—hypo-acousis merely, or a severe complex of symptoms similar to Ménière's syndrome, consisting of tinnitus aurium, deafness, vertigo, vomiting, nystagmus, and disturbances of equilibrium.

The underlying pathology is the posterior poliomyelitis, a specific inflammation of ganglia of the spinal type. The characteristic features are given to this chapter of zona by the proximity of the geniculate ganglion to the facial and the terminal divisions of the auditory nerve, the inflammation in the geniculate ganglion extending to the adjacent nerve trunks by contiguity of structure. The pressure effects would be still further increased by the enclosure of these structures in a common sheath, situated in a narrow osseous canal.

I also believe that the ganglia of the acoustic nerve may be primarily involved, and I have given embryonal, histological, and

clinical grounds for advancing this theory. I have also suggested the possibility of the ganglia of the glossopharyngeal and vagus nerves playing a role in the symptomatology of the syndrome, and emphasized the great importance, clinically, of vagus symptoms in this relation.

A particular emphasis has also been given to the occurrence of mild inflammatory reactions in ganglia above or below the chief focus, or that giving rise to the eruption of herpes zoster (*eruptive focus*). The symptoms present in the non-eruptive zones are mild and transitory in nature, and consist of pains and slight objective sensory disturbances. I regard the Gasserian, geniculate, acoustic, glossopharyngeal, vagus, second, third, and fourth cervical ganglia as representing a continuous ganglionic series or chain, all having the same embryonal origin (*neural ridge*), and all, with the exception of the acoustic ganglia, having the same cell type (unipolar), and therefore belonging to the realm of posterior poliomyelitis. This serial chain of ganglia is concerned in the production of the syndrome. A hemorrhagic inflammation in one of these ganglia is followed by the usual manifestation of herpes zoster, an eruption appearing in its respective zone.

Depending upon the severity of the infection, other ganglia of the group may be the seat of an inflammatory reaction as well, but not sufficient in degree to produce an eruption. This milder involvement is manifested clinically by pains and slight objective sensory disturbances, and in the case of the geniculate and acoustic ganglia, by their respective neural symptoms.

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## THE PRESENT STATUS OF EXPERIMENTAL ARTERIAL DISEASE.<sup>1</sup>

BY I. ADLER, M.D.,  
OF NEW YORK.

FOR a long time the problems, both clinical and pathological, involved in the question of arteriosclerosis have received considerable attention on the part of the investigator, the clinician, and the practitioner. The saying that "a man is as old as his arteries" has become public property, not only of the medical, but also of the lay world, and passes almost as an axiom today.

An enormous literature has sprung up on arteriosclerosis, and it has been attacked by many brilliant and indefatigable workers from the clinical and histological as well as from the experimental

<sup>1</sup> Read at a meeting of the New York Academy of Medicine, March 19, 1908.

side, without, however, it must be confessed, any unanimity of view or clearness of conception being attained. It was, therefore, hailed by many as the beginning of a new era in the study of arteriosclerosis when Josué,<sup>2</sup> in 1903, reported that he had artificially produced arteriosclerosis, or, as he called it, "atheroma," in the aorta of rabbits by intravenous injections of adrenalin. The matter was at once taken up by investigators in many countries. Erb,<sup>3</sup> Külbs,<sup>4</sup> Kurt Ziegler,<sup>5</sup> v. Rzentkowski,<sup>6</sup> Fischer,<sup>7</sup> Scheidemantel,<sup>8</sup> D'Amato,<sup>9</sup> Pearce and Stanton,<sup>10</sup> Lissauer<sup>11</sup>, Baylac and Albarede,<sup>12</sup> Biland,<sup>13</sup> and others have in the main verified and somewhat added to Josué's results.

The lesions thus produced are very characteristic, and on superficial view seem to resemble closely atheromatous degeneration in the human aorta. Their site of predilection is the ascending portion and the arch of the aorta; in more advanced cases the descending portion is involved. The abdominal aorta is the last to suffer, and extensive lesions there are rather exceptional. A few cases, however, have been reported in which the entire aorta from its origin down into the iliacs has been converted into a rigid tube of degeneration.

The lesions appear as larger or smaller patches of peculiar translucent appearance and rough surface; in the advanced stages the edges are somewhat raised above the level of the inner surface of the vessel, while the centre is usually depressed; the vascular walls are distinctly thinner than normal in and about these patches, and thus tend to the formation of aneurysmatic dilatations and pouches. It should be noted that the aneurysmatic dilatation never involves the entire circumference of the vessel, but is a partial bulging corresponding to the location of more or less intensely degenerated patches. Erb, Fischer, and Ziegler have noted cases of dissecting aneurysm. As a rule, calcification appears at a very early stage of the process.

<sup>2</sup> Atherome aortique expérimentale, *Presse médicale*, 1903, 1904, p. 798.

<sup>3</sup> Experimentelle und histologische Studien über Arterienerkrankung nach Adrenalininjektionen. *Arch. f. exp. Path. u. Pharm.* 1905, liii, 173.

<sup>4</sup> Experimentelle Studien über die Wirkung der Nebennierenextrakte. *Arch. f. exp. Path. u. Pharm.*, 1905, liii, 140.

<sup>5</sup> Ueber die Wirkung intravenöser Adrenalininjektionen auf das Gefäßsystem und ihre Beziehung zur Arteriosklerose. *Ziegler's Beiträge*, 1905, xxxviii, 229.

<sup>6</sup> Atheromatosis aortae bei Kaninchen nach intravenösen Adrenalininjektionen. *Berl. klin. Woch.*, 1904, 830.

<sup>7</sup> Ueber Arterienerkrankungen nach Adrenalininjektionen. *Kongress f. innere Medizin*, 1905, 236.

<sup>8</sup> Ueber die durch Adrenalininjektionen zu ersengende Aortenverkalkung der Kaninchen. *Virchow's Arch.*, 1905, clxxxi, 363.

<sup>9</sup> Weitere Untersuchungen über die von den Nebennieren Extrakten bewirkten Veränderungen der Blutgefäße und anderer Organe. *Berl. klin. Woch.*, 1906, Nrs. 33, 34.

<sup>10</sup> Experimental Arteriosclerosis. *Jour. Exper. Med.*, 1906, viii, 74.

<sup>11</sup> Experimentelle Arterienerkrankungen beim Kaninchen. *Berl. klin. Woch.*, 1905, p. 675.

<sup>12</sup> Recherches expérimentales sur l'atherome de l'aorte consécutif à l'action de l'adrenaline. *Compt. rend. de la soc. de biol.*, 1904, lvii, 640.

<sup>13</sup> Ueber die durch Nebennieren präparate gesetzten Gefäß und Organveränderungen. *Deut. Arch. f. klin. Med.*, 1906, lxxxvii, 1906, p. 413.

The yellow patches of fatty degeneration and the so-called gelatinous patches, so frequent and constant in human atheroma, have, so far as I know, never been found in these experimental affections of the rabbit's aorta, nor do the patches just described ever seem to lead to ulceration.

Almost all investigators have found these lesions confined to the aorta, no matter how long the animals have been subjected to treatment. Erb, it is true, reports some lesions in other vessels, iliacs and carotids, but no other observer has been fortunate enough to meet with similar results. Once or twice slight degeneration of the pulmonary artery has been noted. The fact that many rabbits subjected to intravenous injections of adrenalin die very suddenly of cerebral hemorrhage suggests the strong probability of damage to the smaller cerebral vessels, but as yet no one has been able to detect any palpable lesions.

All observers are pretty well agreed on the histology of these lesions. The degeneration is primarily and mainly located in the media. The first change that occurs is necrosis of the smooth muscle cells, and as they are destroyed, the elastic fibers, deprived of the support of the muscle cells and no longer able alone to withstand the pressure, are first stretched to their utmost limit and then snapped and broken. There is still some doubt whether the elastic fibers themselves degenerate, although it is probable that, together with the tension and the metabolic changes going on within the vessel wall, some fatty degeneration of the elastic fibers does take place. Calcareous deposits very soon appear within the areas of necrotic and destroyed cells and fibers. No inflammatory process can be observed during all these changes. Leukocytic emigration in the outskirts of the patch, with an occasional giant cell, is occasionally seen, but only after calcification is complete or nearly so. The whole is distinctly a necrotic and not an inflammatory process, and is in the main strictly confined to the media. The intima seems not to be largely involved. In those places where considerable depression occurs together with distention of the vessel wall, some hypertrophy of the intima takes place, but degeneration or ulceration of the intima has not been observed.

It was very soon found that the suprarenal extracts—adrenalin, suprarenin, perinephrin, and others—were not the only substances that produce the peculiar effects in the aorta of rabbits. A number of other substances that tend to raise blood pressure produced the same results. Fischer obtained positive results with digalen, Miller<sup>14</sup> with barium chloride, Bennecke<sup>15</sup> with barium chloride, hydrastin, and hydrastinin, Sturli<sup>16</sup> with methylamino-acetobrenzkatechin,

<sup>14</sup> Experimental Arterial Degeneration. *AMER. JOUR. MED. SCI.*, 1907, p. 593.

<sup>15</sup> Studien über Gefässerkrankungen durch Gifte. *Virchow's Arch.*, 1908, xcxi, 202.

<sup>16</sup> Gefäßveränderungen nach Injektionen von Methylamino-acetobrenzkatechin. *Münch. med. Woch.*, 1905, 630.

which is also a vasoconstrictor and pressure raiser. Some years ago I<sup>17</sup> fed tobacco infusion to rabbits, with a view of testing the effect on the bloodvessels. Interesting changes in the liver and in the smallest vessels were found, but none in the aorta. After the appearance of Josué's paper, in association with Dr. Hensel,<sup>18</sup> I injected pure nicotine, also a decided blood pressure raiser, into the ear vein of rabbits, with positive results. Miller also obtained positive results with nicotine. Boveri<sup>19</sup> obtained positive results with infusion of tobacco by the mouth. Gouget<sup>20</sup> treated rabbits with infusion of tobacco by the mouth and intravenously and with a combination of both. Baylac<sup>21</sup> obtained positive results by intravenous as well as by subcutaneous administration of tobacco infusion. Quite recently Rickett<sup>22</sup> evidently unaware of our experiments, obtained positive results with nicotine and with infusion of tobacco intravenously.

All the substances mentioned thus far have one quality in common—they are more or less decided raisers of blood pressure; and the conclusion naturally suggests itself that the effect obtained is produced by the blood-pressure-raising quality of the drugs employed. This fits in very nicely, too, with the prevailing theories of human arteriosclerosis, and many authors build far-reaching theories and hypotheses on this basis. A closer scrutiny of the facts shows this view, however, to be untenable.

Mironescu<sup>23</sup> experimenting with euphthalmin, which is said to depress blood pressure as violently and suddenly as adrenalin raises it, comes to the conclusion that it is not the rise in blood pressure, but the sudden variations in pressure that produce the effect. D'Amato experimented with paraganglin, which, as he proved by manometric tests, does not raise the blood pressure. The paraganglin was given intravenously as well as by the mouth, and he obtained results similar to those with adrenalin. When given by the mouth it was necessary to employ much larger doses. D'Amato is inclined to look upon the action as purely toxic, and claims a special affinity of paraganglin for the smooth muscle, he having found slight degrees of necrosis in the muscles of the stomach and intestine, as also in the bladder, when given by the mouth. Braun<sup>24</sup> gave amyl

<sup>17</sup> Some Effects of Tobacco on the Tissues of Rabbits. *Jour. Med. Research*, viii, No. 2.

<sup>18</sup> Intravenous Injections of Nicotine and Their Effects upon the Aorta of Rabbits. *Jour. Med. Research*, September, 1906, v, No. 2.

<sup>19</sup> Contributo allo Studio degli Atheromi aortici sperimentali. *Clinica med. Ital.*, 1906, xiv, 41.

<sup>20</sup> Sur quelques lésions de l'intoxication tabagique expérimentale. *Presse méd.*, 1906, No. 67, 533.

<sup>21</sup> Athérome expérimental de l'aorte consécutif à l'action du tabac. *Compt. rend. de la Soc. de biol.*, 1906, ix, 935.

<sup>22</sup> Experimental Atheroma. *Jour. Path. and Bact.*, October, 1907, xii, No. 1.

<sup>23</sup> Beiträge zur Wirkung des Adrenalins und Euphthalmins auf den Blutdruck beim Kaninchen. *Zentralbl. f. innere Med.*, 1906, 598.

<sup>24</sup> Zur Frage der Arteriosklerose nach intravenöser Adrenalinzufuhr. *Münch. med. Woch.*, 1905, p. 533.



nitrite and adrenalin together intravenously and obtained positive results, though he had shown by careful manometric measurements that this combination does not alter the blood pressure; he is, therefore, convinced that the positive results obtained were caused by toxic action. Fischer obtained positive results with a great variety of substances, a large number of which, such as acids, ferments, and even normal saline, had little or no effect upon blood pressure. Kolisch<sup>26</sup> claims positive results with phloridzin and phloretin, both of which are said to have no effect on blood pressure. Boveri injected carbonate of lead in physiological salt solution in three rabbits, and found dilatations, thickenings, calcifications, and aneurysms. He also experimented on 6 rabbits with putrid material, partly through a stomach tube and partly subcutaneously, obtaining positive results in three, while the other three showed no lesions. Fischer writes that he has produced aneurysms without calcification and with but very little change apparent to the naked eye in rabbits by the injection of various metallic salts. (I have been unable to find any detailed account of these experiments.) It might be mentioned in this connection that Koranyi<sup>28</sup> claimed that iodine, especially in the form of iodipine, inhibited the action of adrenalin on the rabbit's aorta. As this seemed to supply an experimental basis for the popular treatment of arteriosclerosis, it created quite a sensation. It was tested by many, especially by Loeb and Fleisher<sup>27</sup> who, after very careful experiments on a large number of rabbits, could find no palpable influence of the iodides upon the action of adrenalin. This seems now to be the general opinion. In a later publication Koranyi<sup>28</sup> claims that it is not the iodine, but the oil, which tends to neutralize the effect of the adrenalin.

Morelli<sup>29</sup> a pupil of Koranyi, working with digalen, finds that sesame oil prevents its action upon the rabbit's aorta. According to Bennecke, spermin counteracts to some extent the action of hydrastinine. On the other hand, Hedinger and Loeb<sup>30</sup> encountered the typical aortic lesions in rabbits treated with subcutaneous injections of KI, but all their further experiments with the iodides proved negative. We should mention also the work of Loeb and Githens<sup>31</sup> concerning the effect of intravenous injections of adrenalin

<sup>26</sup> Ueber durch Phloridzin hervorgerufene Aortenveränderungen. Münch. med. Woch., 1905, p. 2446.

<sup>27</sup> Ueber die Wirkung des Iods auf die durch Adrenalin erzeugte Arterionekrose. Deutsch. med. Woch., 1906, Nr. 17.

<sup>28</sup> Ueber den Einfluss von Iodpräparaten auf die durch Adrenalininjektionen hervorgerufenen Gefäßveränderungen. Deutsch. med. Woch., 1907, Nr. 10, 382.

<sup>29</sup> Berichtigung zu meiner Mitteilung über die Wirkung des Iods auf die durch Adrenalin erzeugte Arterionekrose. Deutsch. med. Woch., 1907, Nr. 5.

<sup>30</sup> Ueber Arterionekrose. Berl. klin. Woch., 1908, Nr. 8, 398.

<sup>31</sup> Ueber aortenveränderungen bei Kaninchen nach subkutaner Iodkaliverabreichung. Arch. f. exp. Path., 1907, lvi, 314.

<sup>31</sup> The Effect of Experimental Conditions on the Vascular Lesions Produced by Adrenalin. AMER. JOUR. MED. SCI., October, 1905, 403.

in rabbits with experimental nephritis, in others after thyroidectomy, and in pregnant animals, with a view of testing the effect of these injections both on the mother and on the developing bloodvessels of the fœtus. They also studied the effect of pyrokatechin.

We have thus a rather large group of substances, some tending to raise blood pressure, some having no effect at all upon it, some few even lowering it, but all producing very similar, it may be said practically identical, effects upon the aorta of rabbits. They all primarily affect only the media, causing necrosis with degeneration and calcification of the smooth muscle fibers, stretching and breaking up of the elastic fibers, and, when the intima is at all affected, it is simply in the form of more or less secondary and compensatory thickening, never associated with any degeneration or ulceration, the entire process resembling that described by Mönckeberg<sup>22</sup> in human peripheral vessels.

In order to arrive at a just valuation of these experimental results a number of other facts must be noted. In the first place, it must be stated that the lesions described have been obtained only in rabbits. All efforts to produce similar affections in other animals, as dogs (Pearce and Stanton, Fischer, v. Rzentkowski, and others) and monkeys (Erb), have utterly failed. Even in rabbits, however, there is apparently no constancy or regularity in the effect, and it is impossible to predict the result of any experiment, no matter what substance is used.

Kaiserling<sup>23</sup> experimented on 8 rabbits with adrenalin, one of which received as many as 66 injections, with absolutely no macroscopically visible lesions, and under the microscope nothing was to be seen except a slight stretching of the elastic fibers.

It is to be regretted that many observers give no details of their experiments, but all that do, report a varying number of negative as well as positive results. Again, it is generally recognized that the positive results obtained are very frequently in no proportion to the number of injections or to the duration of the experiment. Erb has seen extensive calcification of the entire aorta down to the iliacs after one single injection of adrenalin. It is a common experience to have extensive calcareous patches after but comparatively few injections, and no lesions after numerous injections and prolonged treatment. Adler and Hensel found calcification and aneurysms after only 18 injections of nicotine, and no gross lesions whatsoever after as many as 117 nicotine injections.

Josué called attention to the fact that the age and weight of the rabbit are important factors; that the results are more likely to be positive in old animals than in young ones. This seems, on the

<sup>22</sup> Ueber die reine Mediaverkalkung der Extremitätenarterien und ihr Verhalten zur Arteriosklerose. *Virchow's Arch.*, 1903, clxxi, 141.

<sup>23</sup> Beiträge zur Wirkung intravenöser Suprarenininjektionen auf die Kaninchenaorta. *Berl. klin. Woch.*, 1907, Nr. 2, 29.

whole, to be borne out by the results of subsequent research. Pic and Bonnamour<sup>34</sup> injected two young rabbits, weighing under 2000 grams for three months with adrenalin, with no visible effect. Older and heavier animals weighing over 2000 grams gave positive results after a comparatively short time. They found too, that rabbits artificially made tuberculous, or whose power of resistance was impaired, for example, by lactation, responded more readily to adrenalin. Their experiments, however, are too few in number to be convincing. Fischer, however, arrives at similar conclusions.

On the other hand, there are reports of old animals showing nothing, and of young animals with positive results. Thus, Kurt Ziegler found calcareous patches in the abdominal and thoracic aorta with aneurysmatic dilatation in a rabbit only eight weeks old that had been injected only for ten days, while an old animal that had been injected with adrenalin intravenously for six and a half months and subcutaneously for another three and a half months, the entire experiment lasting ten months, showed no gross lesions and but very slight microscopic changes.

In view of these irregular and contradictory results, the question suggested itself to many investigators: Are we really producing an experimental effect by our intravenous and subcutaneous injections? Is it not possible, nay, even probable, that our so-called positive results are the natural outcome of spontaneous disease of the rabbit, and have no relation whatever to our experimental treatment?

It is beyond doubt that arterial disease does occur spontaneously in animals. Lyding,<sup>35</sup> for instance, finds in the ox and in the horse aortic disease very much like human arteriosclerosis, and in the dog a condition in many respects similar to the lesions in the rabbit's aorta. The necessity for investigating this question in the rabbit is obvious. Hedinger and Loeb examined about 100 rabbits that had not been used for experimental purposes, but could find no gross aortic lesions. Von Rzentkowski examined 10 rabbits, with the same negative result; Adler and Hensel, 14 rabbits, all fully grown, some of them old and all weighing over 2000 grams, without being able to detect any macroscopic lesions in the aorta. Fischer states positively that he has found in a number of rabbits (he gives no figures), especially in such as have died from some form of cachectic disease, spontaneous aortic lesions exactly identical, macroscopically and microscopically with those found after adrenalin injections. Bennecke examined 400 rabbits not used for experiment, and found typical aortic lesions of various degrees of intensity in 12 (3 per cent). Quite recently Amy B. Miles<sup>36</sup> published some very startling

<sup>34</sup> Contribution à l'étude du déterminisme de l'atherome aortique experimental. Soc. de Biol., 1905, 219.

<sup>35</sup> Zur Kenntnis der Arteriosklerose bei Hausthieren. Zeits. f. Tiermed., Band ii, p. 359.

<sup>36</sup> Spontaneous Arterial Degeneration in Rabbits. Jour. Amer. Med. Assoc., October 5, 1907, p. 1173.

figures: 61 rabbits were treated with intravenous injections of adrenalin; of these, only 17 (27.86 per cent.) showed macroscopically visible lesions. Of 49 normal rabbits obtained from the same source, kept under the same conditions, and not experimented upon, 17 (34.77 per cent) showed macroscopic lesions. (Nothing is mentioned concerning age and weight of the animals.) The lesions in both sets were identical and of the usual type. When one considers the many thousands of rabbits that have been used for experiment and dissection, it is certainly astonishing, in the light of the statistics of Dr. Miles, that spontaneous aortic disease has not more often been encountered before this. Possibly these lesions may frequently have been overlooked, no special attention being paid to the condition of the vascular system. It is highly probable that breed, environment, food, age, and general condition are important and insufficiently studied factors concerned in the development of spontaneous aortic lesions in the rabbit. That, however, aortic lesions do occur spontaneously in rabbits, and more often than one would have imagined, seems certain.

The experiments dealing with bacteria and their toxins had best be grouped into a separate class. They are as yet but few in number, but promise, if continued, most valuable results. The changes found in the rabbit's aorta in most of these experiments are said to be different from the adrenalin type, and to resemble more nearly human arteriosclerosis. Thus Gilbert and Lion<sup>37</sup> as early as 1889, injected typhoid bacilli into the ear vein of a rabbit whose aorta had previously been injured. They found at the place of injury a plaque surrounded by a zone of inflammatory material involving both the intima and the media, with a central depression and calcification, particularly in the media. In another rabbit whose aorta had not been injured, injected with a malignant bacillus isolated from man, they found also a plaque in the aorta, but no calcification; there was a distinct hyperplasia of the intima almost purely of connective tissue. They state distinctly that in location, in gross appearance, and in histological structure it approached very closely the arteriosclerosis of the human aorta, and they consider their experiments a proof that infectious disease may be the cause of arteriosclerosis. O. Klotz,<sup>38</sup> besides experimenting with adrenalin under various conditions, and in the main verifying the results of others, obtained important results with the typhoid bacillus and the streptococcus. These, injected into the ear vein of rabbits, seemed to produce changes in the aorta and in the *pulmonary artery* closely resembling the conditions found in arteriosclerosis of the human aorta. There were no aneurysms and no calcification, but fatty degeneration of the endothelial cells

<sup>37</sup> Arterites infectieuses expérimentales. Compt. rend. Soc. de Biol., 1889, p. 583.

<sup>38</sup> A Discussion on the Classification and Experimental Production of Arteriosclerosis. Brit. Med. Jour., 1906, p. 1767.

and a hyperplasia of connective tissue taking the place of the degenerated material. He also described splitting of the external elastic lamina similar to that described by Jores in human vessels. The injection of diphtheria toxin seemed to affect only the first portion of the aorta and produce lesions similar to those produced by adrenalin.

The earlier experiments, in which injuries, mechanical and chemical, were applied to the vessels, do not concern us here, nor shall I consider the experiments of Lewaschew, Fränkel, and Barvoets, who produced extensive lesions in vessels by resection of nerves (sciatic nerve). Von Czyhlarz and Helbing<sup>39</sup> have conclusively shown that the lesions produced by these observers are of a purely inflammatory character and will not ensue if all inflammation is prevented.

Returning to the aortic lesions of the adrenalin type, there has been much discussion as to the mechanism by which these lesions are produced, more especially whether increased blood pressure—hypertension—or toxic influences are to be held responsible. If we accept the view that the lesions in question are really produced by the substances introduced into the circulation, then the theory that hypertension is the sole or even the main factor in the process seems untenable. The mere fact that similar results have been obtained by substances tending to lower blood pressure, as well as by others that have no influence whatever upon pressure, is sufficient to upset the hypertension theory. It is, besides, hardly conceivable that a sudden, even a very considerable, rise of pressure, if of short duration, could cause such extensive changes. Josué,<sup>40</sup> it is true, claims that repeated injections of adrenalin keep up the pressure above normal for a long time. This is denied by others. That toxic influences are at work is proved not only by the known toxic character of many of the chemicals employed, but also by the cachexia which frequently appears, and the marked toxic and irritant lesions found in other organs besides the aorta, such as the liver, the heart, the kidneys, etc., which it is not within the scope of this paper to describe. Even adrenalin, besides its pressure-raising quality, has a distinctly toxic influence on various organs and also on the blood itself, according to Loeper and Grouzon.<sup>41</sup>

In view, however, of the startling figures brought forward by Miles, and after deliberate and careful study of all the results, both positive and negative, at present available, it may well be questioned if the aortic lesions observed are the result of experiment, or if they are not rather simply the natural outcome of spontaneous disease without any causal relation to experimental procedures. Klotz has

<sup>39</sup> Experimentelle Untersuchungen über die Beziehung von Nervenlesionen zu Gefäßveränderungen. *Centralbl. f. Path. u. path. Anat.*, 1897, viii, 849.

<sup>40</sup> La pression artérielle chez le lapin à la suite d'injections répétées d'adrenaline dans les veines. *Soc. de Biol.*, 1905, 319.

<sup>41</sup> L'action de l'adrenaline sur le sang. *Arch. de med. exp. anat. et path.* 1904, p. 83.

shown that long before macroscopic lesions become visible minute degenerations of the muscle cells and elastic fibers, even the beginnings of calcification, may exist. It may well be conceived that the toxic elements experimentally introduced into the circulation, if they have any effect at all, act simply as a more or less powerful stimulus upon an already diseased aorta and render active and manifest the pathological condition until then merely latent. A series of experiments by Dr. Hensel and myself, not yet published, on about 100 rabbits, with various toxic substances, taking into account the numerous negative as compared to the positive results, has suggested this conclusion to us even before the publication of Dr. Miles' paper. Fischer seems to entertain similar opinions. In the present state of our knowledge it is perhaps the most plausible solution of the difficulty, but before the question can be finally decided much more investigation will be necessary.

Do these pathological processes as found in the rabbit's aorta bear any relation to human arteriosclerosis? The majority of German authors hold the opinion that they have nothing whatever to do with human arteriosclerosis; others, especially those of the French school, unhesitatingly consider them as identical with human atheroma. Though, of course, it is far beyond the limits of this paper to enter into any details concerning the various theories of arteriosclerosis, or to discuss, no matter how briefly, the innumerable problems—physiological, pathological, histological, and clinical—offered by the vascular system,<sup>42</sup> it will nevertheless be necessary to state in as few words as possible what we conceive to be the present status of our knowledge of human arteriosclerosis, or "atherosclerosis," as it is aptly named by Marchand.<sup>43</sup> There has been a marked tendency, especially since the work of Jores<sup>44</sup> and his followers, to consider, when speaking of arteriosclerosis, mainly the characteristic lesions in the aorta, and to relegate to an entirely different class the calcifications and other changes in the media in other arteries, especially in the peripheral vessels, as described by Mönckeberg. This view is perhaps, as Klotz remarks, too narrow in its limitations. The clinical manifestations of arteriosclerosis are not as yet as sharply defined in all their details as may be desirable, but there is a vivid and distinct conception of human arteriosclerosis in the mind of every physician, and though perhaps somewhat loosely handled at times, is nevertheless a clinical entity dealing with the vascular system as a whole, and not merely with the aorta.

It may then be said very concisely, with Aschoff,<sup>45</sup> that the essential

<sup>42</sup> A full discussion of the pathology of arteriosclerosis and its more recent literature is given by Thorel, Lubarsch, and Ostertag, *Ergebnisse*, 1903, 1; 1907, ii.

<sup>43</sup> Ueber Arteriosklerose. *Kongress f. innere Medizin*, xxi.

<sup>44</sup> Wesen und Entwicklung der Arteriosklerose, 1903.

<sup>45</sup> Ueber Atherosklerose und andere Sklerosen des Gefäßsystems. *Beihefte z. med. Klinik*, 1908, iv, Nr. 1.

and cardinal point in the pathology of atherosclerosis is impairment and subsequent degeneration of the elastic elements. Atherosclerosis is mainly a hyperplastic and degenerative, and in no wise an inflammatory process. Endarteritis proliferans and obliterans, though often, no doubt, associated with true atherosclerosis, must be classed separately. The same holds good for certain specific infections, especially syphilis. The latter may perhaps be a factor in bringing about general arteriosclerosis, but the easily recognized and characteristic luetic lesions as they appear in the aorta and the cerebral vessels must be separated from typical arteriosclerosis.

It is being more and more clearly recognized that different vessels have different functions, and, therefore, also different structure, and perform their work under different physical and mechanical, and possibly different chemical conditions. The aorta, for instance, especially the ascending portion, receives every moment a large volume of blood direct from the heart under high pressure and with undoubtedly numerous cross-currents and vortices, for which it must provide an even distribution. The femoral, on the other hand, at great distance from the heart, must pass the blood to the smaller arteries with sufficient force and impetus to secure uniform tension down to the capillaries. Aschoff\* divides all arteries into two groups according to their differences in structure: those of the elastic type, aorta, carotids, and iliacs, and those of the muscular type, the majority of the peripheral arteries. In vessels of the elastic type, whose most important function it is to withstand pressure and prevent overdistention, the intima with its elastic and connective tissue elements is the more important factor; while in vessels of the second group, that have special propelling functions, the muscular elements of the media are more highly developed. It is conceivable that physical strain, toxic influences, and the like may cause different reactions in different vessels according to their type of structure and of function.

Ever since Thoma's investigations the growth and development of the bloodvessels has been the object of considerable careful research. It is generally accepted now that there is a continuous increase in length as well as a regular and progressive development of the structural elements of the aorta and larger vessels, especially of the connective and elastic tissue of the intima. With the increased demands on the vessel, reinforcements of the elastic and fibrous and also of the muscular elements keep equal step, so that under the influence of normal conditions of pressure and longitudinal and lateral tension, what may be called a physiological hyperplasia of the intima takes place. This physiological process of growth reaches its climax usually in the third decade of life. The very

\* Generally speaking, arteries may be conceived as consisting of two concentric tubes: an inner fibro-elastic tube and an outer muscular tube.

valuable and exact measurements of Scheel<sup>47</sup> corroborate the results obtained by others (Bennecke and Suter). According to these investigators the completion of normal growth is followed almost immediately by the first signs of regression. Thayer and Fabyan<sup>48</sup> have come to similar conclusions from histological studies of the radial artery. Slowly but surely the elasticity of the arteries begins to decrease, the vessels to dilate somewhat; in other words, the first faint senile changes appear very soon after maturity is reached, and lead, in some individuals sooner, in others later, inevitably to arteriosclerosis.

There is almost a consensus of opinion that pressure and tension are the main factors in the development both of the physiological and the pathological alterations in the arteries, and that, as Albrecht<sup>49</sup> puts it, mechanical impairment is the underlying and primary cause of arteriosclerosis. That hard physical labor and strain tend to accelerate the normal "physiological" advent of arteriosclerosis seems more than likely. Thayer and Brush,<sup>50</sup> in an analysis of the records of nearly 4000 cases, find that heavy physical labor gives a very high percentage of palpable radial arteries. Baumler<sup>51</sup> records the interesting observation that left-handed persons often develop arteriosclerosis of the left radial, the right being normal. But arteriosclerosis is not merely the result of overstrain, of wear and tear of the arteries; is not merely an "Abnutzungs-Krankheit," as the Germans call it. There must be, beyond doubt, other and probably numerous factors tending to impair the elasticity and lower the power of resistance of the vascular walls. We cannot close our eyes to the fact that we find every now and then some fortunate ones who live to a high old age, often under great stress and strain, without showing until almost the very end of life any very marked symptoms of arteriosclerosis. On the other hand, arteriosclerosis is found with increasing frequency, as more attention is paid to the subject, in youthful individuals. Without attaching too much importance to the well-known case of Bryant and White,<sup>52</sup> in which all the arteries of the body with the exception of those of the head were sclerotic and calcified, or the case of Durante,<sup>53</sup> in which atheroma of the pulmonary artery was found, evidently prenatal, in a seven months child that died of umbilical infection shortly after birth, there are the figures of

<sup>47</sup> Gefässmessungen und Arteriosklerose. Virchow's Arch., 1908, xcxi, Heft i, Nr. 1.

<sup>48</sup> Studies in Arteriosclerosis, with Special Reference to the Radial Artery. Trans. Assoc. Amer. Physicians, 1907, xxii, 694.

<sup>49</sup> Über Arteriosklerose. Münch. med. Woch., 1906, 332.

<sup>50</sup> The Relation of Acute Infections to Arteriosclerosis. Jour. Amer. Med. Assoc., 1904, p. 726.

<sup>51</sup> Ist die Arteriosklerose eine Allgemein Krankheit. Berl. klin. Woch., 1905, Nr. 44a.

<sup>52</sup> A Case of Calcification of the Arteries, etc., in a Child aged Six Months. Guy's Hospital Reports, lv, 18.

<sup>53</sup> Bulletin de la Soc. Anat. 1899, p. 97.



v. Simnitzky,<sup>54</sup> who has confined his attention only to the aorta, but finds the early stages of arteriosclerosis in individuals under twenty-five years of age in at least 27.5 per cent. of all cases examined.

Huchard<sup>55</sup> and his school make the acute infectious diseases of infancy and childhood largely responsible for the arteriosclerosis of later years. Hofbauer<sup>56</sup> saw arteriosclerosis following measles in a boy aged seventeen years. The studies of Thayer<sup>57</sup> and of Thayer and Brush<sup>58</sup> tend to show that, besides hard work, typhoid fever and alcoholism have a marked effect upon the early development of arteriosclerotic symptoms. Richard Wiesner<sup>59</sup> frequently found extensive calcification in the coronaries of youthful individuals between the ages of fifteen and twenty-three years after endocarditis or prolonged osteomyelitis. Wiesel<sup>60</sup> made extensive studies of the heart and bloodvessels of youthful persons in many of the infectious diseases—typhoid fever, scarlet fever, measles, diphtheria, sepsis, pneumonia, osteomyelitis, etc. He found lesions in the arteries mainly in the media and in many respects resembling experimental lesions in rabbits. According to Lortat and Sabareanu<sup>61</sup> diseases of the thyroid gland and thyroidectomy have a decided effect upon the early and extensive development of arteriosclerosis. That alcoholism, lead, tobacco, and other intoxications tend toward the development of arterial lesions is highly probable, though not as yet positively proved. Gout and diabetes may also be mentioned as causing a marked disposition toward arteriosclerosis. According to Romberg,<sup>62</sup> purely psychic and emotional factors, by causing frequent, rapid, and very violent oscillations of pressure, tend in the same direction. Rumpf,<sup>63</sup> M. Fränkel,<sup>64</sup> Burwinkel<sup>65</sup> and Gazert<sup>66</sup> collect evidence to show that metabolic and chemical disturbances, both local and systemic, are often concerned in the process. Chronic nephritis has long been recognized as a cause of arteriosclerosis. Lastly, clinical observation points to hereditary disposition as an important etiological element.

<sup>54</sup> Ueber die Häufigkeit von Arteriosklerotischen Veränderungen in der Aorta jugendlicher Individuen. *Ztschr. f. Heilkund.*, 1903, xxiv, 177.

<sup>55</sup> Les causes de l'arterio-sclerose et des cardiopathies arterielles. *Rev. gén. de clinique et de thérapeutique*, 1891.

<sup>56</sup> *Wien. klin. Woch.*, 1903, Nr. 34.

<sup>57</sup> The Effects of Typhoid Fever on the Heart and Vessels. *AMER. JOUR. MED. SCIENCES*, March, 1904.

<sup>58</sup> Relations of Acute Infections to Arteriosclerosis. *Jour. Amer. Med. Assoc.*, 1904, p. 26.

<sup>59</sup> Ueber Veränderungen der Koronargefäße bei Infektionskrankheiten. *Wien. klin. Woch.*, 1906, p. 725.

<sup>60</sup> Ueber Gefäßveränderungen im Verlaufe akuter Infektionskrankheiten. *Wein. med. Woch.*, 1906, p. 15; Ueber Veränderungen am Zirkulationsapparate, speziell des peripheren Gefäß-systemes bei Typhus abdominalis. *Ztschr. f. Heilk.*, 1905, p. 107.

<sup>61</sup> Pathogénie de l'athérome artériel et thyroïdectomie. *Soc. de Biol.* lviii, 444.

<sup>62</sup> Ueber Arteriosklerose. *Kongress f. innere Medizin*, 1904.

<sup>63</sup> Ueber Arteriosklerose. *Münch. med. Woch.*, 1905, p. 46.

<sup>64</sup> Ueber Theorie und Behandlung der Arteriosklerose. *Wien. klin. Rundschau*, 1905, p. 30.

<sup>65</sup> Aetiologie und allgemeine Therapie der Arteriosklerose. *Berl. klin. Woch.*, 1905, p. 16.

<sup>66</sup> Ueber den Fett- und Kalkgehalt der Arterienwand bei Atheromatose und Arteriosklerose. *Deut. Arch. f. klin. Med.*, 1899, lxii, 390.

**SUMMARY.** Arteriosclerosis, or, to use the better term, "atherosclerosis," may be designated as a morbid condition of the blood-vessels closely following and allied to the physiological process of development, growth, and senescence of the vascular system, and governed by the same laws. It may without exaggeration be said that atherosclerosis, viewed as a disease, is merely the anticipation in time, extent, and intensity of the normal "physiological" condition of senility. In physiological terms it may be expressed as an impairment or loss of elasticity and of functional adaptability of the vessel walls. Pathologically it is a process of degeneration of the elastic and muscular elements of the vessel walls, associated with compensatory and reparative hyperplasias and hypertrophies principally of the connective tissue elements, and often tending to calcifications and ulcerative processes. The etiological factors that determine its earlier or later onset, its localization, whether more general or more restricted to certain limited portions of the vascular system, and very probably also, at least in part, its histological structure, are manifold. Heredity and physical overstrain ("Abnutzung") in its numerous variations must certainly play an important part. It is most probable that bacterial and other infections, and intoxications with organic as well as inorganic poisons are important etiological factors, and may possibly have considerable influence on the localization as well as on the histological type of the arteriosclerotic process. We are disposed to conceive atherosclerosis, therefore, as a clinical entity. The various types of vascular degeneration briefly mentioned above—the typical lesions in the aorta, the degeneration and calcification in the media of the pulmonary artery, and especially of the peripheral vessels—with all their sequels, are all gathered together into this one large group. They all have a common etiology and are closely allied in their physiological and pathological relations. From this point of view the recent experimental researches with adrenalin, nicotine, and all the other substances would seem to have a direct bearing upon the problem of arteriosclerosis, inasmuch as they appear to demonstrate the effect of toxins of various kinds upon the development of atherosclerotic lesions in the rabbit. They would also appear to go far toward establishing a most important fact, namely, that different kinds of toxic agents can produce lesions of different histological character (bacterial toxins on the one hand and the adrenalin group of poisons on the other). It must be confessed, however, that the element of uncertainty as to how much is due to experiment and how much is spontaneous and independent of all experimentation, which clings to all of these investigations, very seriously impairs the value of all of this work and compels for the present, and until further investigation has cleared up these questions, a suspension of judgment, or at least a very guarded and

provisional acceptance of these results. It may confidently be expected, however, that further research along similar lines, with a study of spontaneous atherosclerosis, especially in carnivorous animals, both wild and domesticated, and its comparison with the human, together with the experimental investigation of the effect of bacterial infection and of toxins on other animals besides rabbits, will materially assist in advancing our knowledge and throwing some light into much that is still very obscure.

## THE BACTERIOLOGY OF THE PUERPERAL UTERUS.

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THE germ content of the uterus has been controversial ground for years. The question has been investigated by many since the time of Doederlein with the most varied results, to be explained, in our opinion, upon the ground of errors in technique. Probably the earliest investigator in this field was Myerhofer, who, in 1865, employed suction by means of a glass tube. He was always able to demonstrate cocci and bacilli if the case were febrile, but he did not find them in afebrile cases. Doederlein, in 1887, reported a series of 30 cases with normal temperature. In 27 of these the lochia was sterile, while in 3 bacilli were present, streptococci being identified once. He drew the conclusions from his study: (1) That in normal cases the uterine lochia is sterile; (2) that microorganisms are almost always present in severe cases of puerperal infection; (3) that infection is not always due to lack of care on the part of the physician. Von Ott and Czerniewski, in 1888, arrived at the same conclusions, but the latter held that the streptococcus might be present in the lochia of normal cases in rare instances without symptoms.

In contradistinction to the above, we wish to call attention to the statistics contributed by Stolz, who found streptococci in the vaginal secretion of three normal pregnant women, while in a series of women with abnormal vaginal secretion during pregnancy streptococci were present in several instances. In studying the puerperal uterus, he found that on the ninth day, in a series of 156

cases examined during labor, with aseptic precautions, there were 55 positive and 101 negative results, streptococci being found in 11 per cent. of the positive cases.

Neither the duration of the labor, the presence of laceration, the number of examinations during labor, or the operations performed to effect delivery seemed to alter the result. Retention of secundines did, however, increase the bacterial content. In 54 women who had not been examined in labor, and in whom the puerperium was normal, he found that in 10, cultures gave streptococci on the ninth day. In a series of over a dozen women in whom cultures were taken on the third, fourth, fifth, sixth, seventh, and eighth day, in order to determine the time of ascendancy of the germs, it was found that early in the puerperium there might be non-pathogenic organisms in the lochia with absence of any signs of infection; that the puerperium from the third day on did not differ in germ content from the later period (ninth day); that the content on the ninth day was less on the average than earlier. Therefore, he believes that in the latter days of the puerperium the uterus cleanses itself from organisms in a large proportion of cases. As his cases were not selected, there occurred a series of 18 in which, one or more days after the culture, there was a development of fever. In this febrile series, with the exception of 5 cases, there had been found a growth in culture before the appearance of the fever, and in half of the positive findings streptococci were demonstrated. In cases in which, on the earliest culture, streptococci were present, there cannot be a question of having caused the fever by infection at the time of culture, according to the opinion of the author. Doederlein and Franz also conclude that in cases of streptococcic vaginal lochia the taking of a culture is not a harmless experiment, but that the infection is sometimes to be laid at the door of the culture. Doederlein declared that the initial period of freedom from symptoms before the taking of the culture could be explained by the incubation of the organisms, but Stolz denies this. However, he does not deny that the presence of streptococci in the cavum uteri may be the cause of the development of fever, without other reason than the trauma necessitated by the culture. He makes the point that the danger is much less if the culture be taken late in the puerperium, and states that he has never seen any difficulty if he has not cultured in the early days. In studying the examination of the lochia and vaginal secretions on the fourth day, he used a series of 75 cases for the uterine lochia and 65 cases for the vaginal secretion. He found that the uterine lochia was positive in 80 per cent. and that in 36.9 per cent. streptococci were present, while the vaginal secretion in 27 per cent. gave streptococci. Both these series were entirely normal cases. He concludes as follows in regard to the findings of the fourth day: (1) That the vagina always contains organisms,

and the uterus does so in a large proportion of cases; (2) that the presence of streptococci in either situation is possible without symptoms; (3) that the uterus contains fewer germs in unexamined cases than in those examined, but streptococci are to be found in both uterus and vagina in some unexamined cases; (4) that examination with sterile hands during labor has no apparent influence upon the germ content; (5) that aseptic glove operations have no distinct influence; (6) that no actual increase in germ content appears to be dependent upon the duration of labor, but that streptococci are relatively increased.

Finally, we would quote rather extensively from the paper of Little, which appeared while this paper was in preparation. Little came to the following conclusions: (1) Cultures taken immediately after labor are sterile in 92 per cent., or in 96 per cent. if gonorrheal cases be included; bacteria may be present exceptionally, even in the absence of vaginal examinations during labor, and the puerperium may be normal; the bactericidal power of the blood serum may be the cause of a certain number of negative results. (In 10 of his 50 cases it was necessary to introduce the hand into the uterus, and it is impossible to believe that no organisms were carried into the cavity. Of course, the downward flow after labor may also be a reason for negative findings in these cases.) Upon the third day he found sterility present in 62.5 per cent. of 40 afebrile cases, as compared with 40 per cent. sterility in 10 cases in which the temperature reached 100.6° or higher. (2) That the inclusion of cases in which gonococci were demonstrated will increase these averages to 85 per cent. and 50 per cent., respectively. (The author calls attention to the fact that he has included in his febrile series cases in which the temperature rise was obviously not due to any intrauterine cause, and the lochia, being sterile in these cases, or at least in some of them, a decrease in the percentage of the negative results is caused in the afebrile series and of the positive results in the febrile.) (3) That the finding of bacteria in the cervical canal at the completion of labor does not necessarily imply their presence later in the puerperium. (In one instance, in which there was a flaw in the tube, the author found a positive result in the first culture, but a negative one the third day, and admits that this was due to contamination with cervical secretion.)

Conclusions based on the cultures made on the seventh day postpartum were as follows: (1) Absolute sterility in 50 per cent. of the afebrile cases, as compared with 20 per cent. of the febrile. (2) Inclusion of gonococci makes these averages 80 per cent. and 50 per cent., respectively. (3) Bacterial findings differ more markedly according as the case is febrile or afebrile than by clinical characteristics. (In 5 of this last series positive results were obtained in cases which had been sterile at both previous cultures.

From 3 of these 5 cases a diplococcus was obtained which resembled, and was probably identical with, the diplococcoid forms so frequently observed in the cervix and vagina, and the author thinks it may have been due to contamination, since he admits that it is impossible to get an absolutely trustworthy result by his method at this stage. In the 2 remaining cases the organisms were gonococci.) It is to be noted that in 20 cases showing bacteria on the seventh day of the puerperium the gonococcus was the organism in 12, and, further, that only 2 of the 10 febrile cases had sterile lochia on the seventh day; the streptococcus found in one instance on the third day had disappeared on the seventh day. (4) The uterus has the power of self-cleansing, and so the presence of organisms on any day of the puerperium does not mean their continued presence, and the author believes that the results given by Stolz, who found fewer organisms late in the puerperium than at an earlier period, are to be thus explained.

The gonococcal findings in his complete series of cases were demonstrated in 2.5 per cent., 25 per cent., and 30 per cent., respectively, on the first, third, and seventh days. His general conclusions as regards the effect of interference during labor are as follows: (1) Laceration of the cervix and the perineum have no bearing upon the germ content of the lochia; and (2) vaginal examinations have but slight effect (4 out of his 6 afebrile cases not examined during labor showed bacteria in the lochia, *Bacillus coli communis* being found once and the gonococcus three times; while 1 afebrile case was examined six times in labor and no organisms were ever found in the lochia.)

Operations to effect delivery resulted in this series as follows: In his febrile series there was one woman who had been delivered by forced accouchement who showed gonococci in the lochia; while a second one, upon whom version had been performed, was the case of streptococcic infection. There were 8 others operated upon in the series, and of them, 3 were positive (version, low forceps, and induced labor, of each, 1 case); 3 other cases showed gonococci (2 low forceps and 1 bag induction); of 2 cases, 1 gave on the third day a variety of *Bacillus dysenteriae*, while the other gave *Micrococcus aureus* and *Bacillus pseudodiphtheriae* on the seventh day (the first was a midforceps operation, and the latter a case of version). The former of these last 2 is considered to have been a contamination at the time of culture.

GENERAL CONCLUSIONS.—In 50 cases studied by Little the uterus was found to be sterile in 92 per cent., 50 per cent., and 44 per cent. on all three days. If gonococci be included, the above averages are 96 per cent., 72 per cent., and 67 per cent. The puerperium is to be noted as normal in 40 and febrile in 10 cases of this series. In the normal cases there was absolute sterility in 92.5 per

cent., 62.5 per cent., and 50 per cent., as compared with the febrile series, in which 90 per cent., 40 per cent., and 20 per cent. were found to be sterile. Including the gonococcic cases, these latter figures would be 95 per cent., 85 per cent., and 70 per cent., and 100 per cent., 50 per cent., and 50 per cent. The author considered his results as positive if bacteria were found only in smear preparations or only in cultures, as well as when present in both. It is likely, therefore, that a certain number of positive results were due to contamination and that the uterus is really sterile in a larger number of cases than these percentages would indicate. Streptococcus was present but once—a febrile case, on the third day; absent, however, on the first and seventh days. Finally, for purposes of completeness, the following schedule of results is worth including, this being taken from Little's article:

					Per cent.
Von Ott	in	9 cases	found lochia sterile in		100
Czerniewski	"	57	"	"	98
Doederlein	"	30	"	"	90
Doederlein	"	250	"	"	83
Vogel	"	15	"	"	80
Franque	"	10	"	"	80
Kronig	"	63	"	"	79
Thomen	"	9	"	"	66
Walther	"	20	"	"	65
Stahler	"	55	"	"	64
Frans	"	10	"	"	0
Burekhardt	"	14	"	"	7
Stahler	"	19	"	"	18
Wormser	"	100	"	"	16
Stolz on the fourth day			"	"	19.6
Vogel	in	15	"	"	34
Schauenstein	"	100	"	"	36
Stolz on the ninth day			"	"	65

The importance of definite and certain knowledge on this whole question cannot be overestimated, because of its bearing upon the general question of puerperal septic infection and more particularly upon the frequency of auto-infection. If some investigators are correct in their findings of pathogenic organisms in a great proportion of normal cases after delivery, it is very evident that the value of this method as an aid to diagnosis is nothing; and, moreover, that auto-infection is one of the most common causes of puerperal sepsis, instead of being, as is the general opinion at present, one of the most rare happenings. Even if the extreme position of Stolz with regard to the frequency of positive findings be found untenable, proof that the ascent of organisms after the first few days into the cavity of the uterus is a usual or even a moderately frequent event will render useless any further consideration of this matter, since the import of positive findings in any given case will be beyond determination.

The probability that streptococci would be satisfied to act as saprophytes within the uterine cavity after delivery being to us a

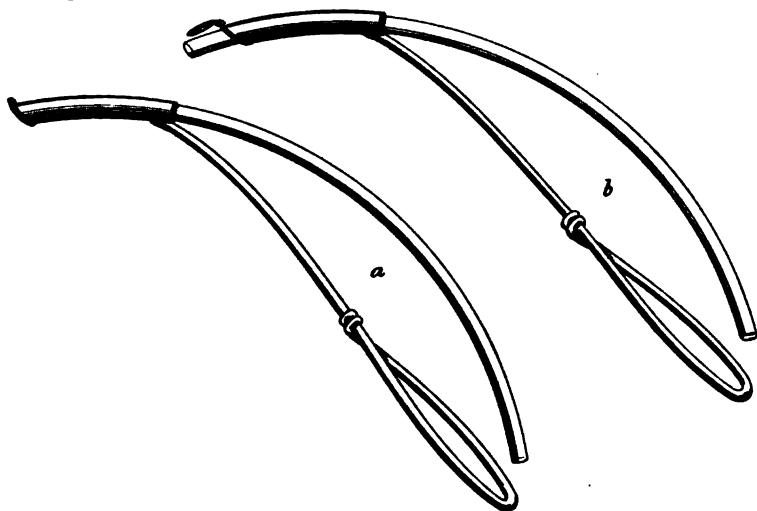
matter of grave doubt, together with the fact that in normal cases, used for demonstration of the method before the class, the laboratory reported pure streptococcic cultures, turned our attention forcibly to the question of the technique employed in the clinic for the collection of the lochia. It being a matter of common knowledge that the lower vagina in most cases is the seat of bacterial activity, and that in a goodly number the same condition prevails in the cervix and upper portion of the vagina, we felt that the method employed, while as careful as any then known to us, demanded modification if it was to be worth doing at all. At this time the ordinary Doederlein tube was employed, sterilized by boiling, and its introduction was performed with the usual aseptic precautions. Realizing that introduction without contamination from the cervix was certainly impossible, if done several days after delivery, and that it was improbable at any time, it was assumed that a positive culture obtained in a normal case simply meant that there was bacterial growth somewhere below the internal os uteri; while those in which this method gave negative results simply gave evidence of both a sterile endometrium and an absence of contamination in the vagina and cervix. Our attention, therefore, was directed toward a modification of the technique which would render possible the collection of uterine lochia without the risk of contamination from the lower canal.

After some experimentation it was decided that there had been several weak points in the technique which we had been in the habit of using, and the method upon which the present findings are based was evolved. Its most important element (see figure) is the use of a slightly curved cervical speculum, the distal end being closed by a hinged cap. A handle of convenient length is attached to render its introduction more easy. We do not claim originality for this idea, as, although at the time the fact was unknown to us, various forms of protective specula have been employed by others. We believe that our instrument will be found to be the simplest as well as the most trustworthy. To enable us to use the speculum, we discarded the typical Doederlein tube and adopted one with a uniform curve and of small caliber, easily obtained from any manufacturer.

The method in detail is as follows: The patient is placed in the lithotomy position and the external genitalia are carefully cleansed with tincture of green soap, water, and mercuric bichloride. A Sim's speculum is inserted, the cervix is grasped by a double tenaculum, and its vaginal portion cleansed with cotton and bichloride solution. The metal tube, with cap closed, is then inserted into the uterine cavity. This tube is sterilized by pressure and wrapped in two coverings, in order that the operator may remove it from the inner one without contaminating his hands. The glass tube is placed within the metal one before sterilization and is not removed



from the latter until the culture has been completed. The cap is opened by pushing the glass tube into the cavity of the uterus, a piece of sterile rubber tubing is attached to the proximal end of the glass tube, and as much lochia as possible is sucked into the glass tube by means of a hard rubber syringe. The glass tube is then withdrawn until its distal extremity is engaged within the metal tube and then both are simultaneously removed from the patient. The ends of the glass tube are sealed with wax and the tube is sent to the laboratory. The points of paramount importance, in our opinion, are the presence of the cap upon the distal end of the sheath tube and the sterilization of the tubes by pressure instead of by boiling. We also feel that the simultaneous introduction of both tubes is very important and that their simultaneous removal is but little less important.



Curved cervical speculum for taking intra-uterine cultures: *a*, tube with cap closed ready for insertion; *b*, after insertion, showing the open cap and the projected inner tube for collecting the secretions.

As important as the collection of the uterine lochia is the technique employed in the laboratory. The danger of outside contamination, especially from the tube itself, must be recognized. For this reason the tube was washed with a bichloride solution, the ends broken off, and the contents placed in a sterile Petri-dish, cultures being made from this upon the following media: (1) Agar-agar stroke plates; (2) glycerin agar stroke plates; (3) serum agar stroke plates; (4) bouillon tubes; (5) litmus milk tubes for anaërobic cultures by Wright's method; (6) glucose agar for anaërobic cultures. In addition, cover slip preparations were made, two being stained with Löffler's stain and two with Gram's stain.

At times this routine method was deviated from because of the

lack of serum agar. This medium was used for the demonstration of the gonococcus. It has been our experience in studying the gonococcus that in the secretions in which the organism could not be demonstrated microscopically no growths occurred upon the special medium used for its cultivation, and that often it could be found in the stained specimen without growth upon the artificial medium, owing to the overgrowth of a mixed culture. For this reason we do not believe that our results as to the presence of the gonococcus are vitiated by the occasional omission of this form of medium. In this series the presence of the gonococcus was remarkably infrequent. We believe this to be due to the technique, which eliminated cervical contamination and proved conclusively to our minds an already formed opinion that gonorrheal endometritis is a much rarer condition than is generally thought. We do believe, however, that this organism is present and persists for a long time in the cervix, often acting as the forerunner of septic infection. Two of the cases in this series showed the presence of the gonococcus; the streptococcus was also found. The frequency with which the gonococcus has been found by other observers we believe to be due to cervical contamination.

In determining the qualifications of a normal case, we have differed from some of the other investigators in this field. We have taken no note of lacerations of either the cervix or the perineum, the duration of the labor, the number of vaginal examinations, the parity of the woman, or the presence of evanescent temperature, unless the latter has been shown clearly to be dependent upon pathological conditions in the generative tract. In other words, we have classified a case as normal if there has been no instrumental interference in labor, if the hand has not been introduced into the uterus, if gauze has not been introduced into the uterus or vagina, and if no douches have been given, if there has been no retention of considerable portions of the placenta or membranes, and if no alteration of the odor or appearance of the lochia has occurred. In short, we use the term normal as descriptive of the most common parturient state. We believe that by so doing we are likely to reach more valuable conclusions than by more closely restricting ourselves in our selection of cases for study, since the important fact for determination is the bacterial content of the uterus in the type of case most usually met with in actual practice.

With regard to the value of the intra-uterine culture as an aid to diagnosis, we feel that it is a method which should not be neglected in the routine study of infected cases, at least in institutions having the advantage of well equipped laboratories of bacteriology. The technique as regards asepsis is more exacting than that required for successful blood culture, since the vagina and cervix, with their bacterial flora, must be traversed in obtaining the intra-uterine culture. If a suitable technique be followed, we are confident that

the results, as a whole, will well repay the time spent in the procedure; but we do not desire to be understood as affirming our belief that the method is, as it was formerly thought, a sovereign means of diagnosing the presence or absence of infection in all cases. We have, for instance, four records not included in this paper, in which in cases afterward proved to be septic, the intra-uterine findings were negative. That such an occurrence will take place as a matter of course, more or less often in a series of examinations of septic cases, must be evident to anyone who will consider the varied manifestations of septic processes during the puerperium. On the other hand, the relative rarity of this negative finding in the presence of septic infection offers valuable evidence as to the general utility of the method.

Taken in connection with the studies upon the bacteriology of the blood which have been made in our clinic, we feel justified in making the following statements: (1) If both blood and intra-uterine cultures are negative, the temperature is due to some intercurrent condition; (2) if the intra-uterine culture is positive, but the blood culture is negative, we consider the infection to be still local in its manifestations; and (3) if the intra-uterine culture is negative but the blood culture is positive—a very unusual condition—we are justified by our general conclusions in considering that the case is one of general infection, the local endometrial condition having been either sterile from the first or having become so gradually after the general infection developed.

It will be noted that we have classified 6 cases as normal which have given cultures in the lochia, and that we have explained the growth in them by errors in technique. We feel that this demands a fuller explanation in order that we may be entirely intelligible. It is necessary that it be clearly understood in the first place that these 6 cases do not include by any means all the cases in which there was a departure from the method described in the first part of this paper. In each instance any such departure was noted at the time the culture was made, and these are the only cases associated with technical error in which a growth was obtained. In the greater number of cases, however, in which accidental departures from the technique occurred, without cultural results, the variation was trivial, being simply noted for reasons of scientific accuracy. In the 6 cases mentioned the variations in the method were of a nature to give expectation of the probability of vaginal or cervical contamination. It is also quite true that the same, or as grave, errors were made in a few cases which did not show positive results in the culture; and this emphasizes our claim that, while a technique as rigid as ours may not always be necessary to obtain satisfactory results in each individual case, still, if error has been made in technique, it is manifestly unfair to consider positive findings as evidence of intra-uterine infection.

## NORMAL CASES—CULTURES TAKEN IN THE FIRST, SECOND, AND THIRD PERIODS.

Number.	Case number.	First period: First to third day.			Second period: Fourth to seventh day.			Third period: Eighth to thirteenth day.			Remarks.
		Aerobic.	Anaerobic.	Microscopic.	Aerobic.	Anaerobic.	Microscopic.	Aerobic.	Anaerobic.	Microscopic.	
1	1	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Normal.
2	2	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Normal.
3	5	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Normal except for one temperature of 102° on the sixth day (a few hours after culture) falling at once to normal.
4	7	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Normal.
5	25	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Student introduced hand into vagina to deliver placenta; otherwise a normal case. On third culture three attempts made before tube passed.
6	56	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Normal.
7	57	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Normal.
8	58	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Normal.
9	61	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Normal.
10	62	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Dead foetus delivered at home; otherwise normal.
	34	See error in technique.			Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Labor normal. Error made at first culture—whereby vaginal secretion obtained.

## NORMAL CASES—CULTURES TAKEN IN THE FIRST AND SECOND PERIODS.

Number.	Case number.	First period: First to third day.			Second period: Fourth to seventh day.			Third period: Eighth to thirteenth day.			Remarks.
		Aerobic.	Anaerobic.	Microscopic.	Aerobic.	Anaerobic.	Microscopic.	Aerobic.	Anaerobic.	Microscopic.	
11	13	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	....	Normal. Febrile temp. once because of congested breasts.
12	27	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	....	Normal.
13	28	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	....	Normal.
14	41	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	....	Normal.
15	42	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	....	Normal.
16	43	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	....	Normal.
17	65	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	....	Normal.
18	6	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	....	Normal.

# NORMAL CASES—CULTURES TAKEN IN THE FIRST AND THIRD PERIODS.

19	9	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
20	14	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
21	15	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
22	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
23	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
24	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
25	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
26	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
27	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
28	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
29	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
30	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
31	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
32	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
33	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.
34	22	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Normal.

# NORMAL CASES—CULTURES TAKEN IN THE FIRST PERIOD ONLY.

26	19	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.
27	60	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.
28	29	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.
29	31	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.
30	44	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.
31	38	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.
32	30	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.
33	64	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.
34	4	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Normal.

# NORMAL CASES—CULTURES TAKEN IN THE SECOND AND THIRD PERIODS.

35	10	....	Sterile.	....	Negative.	Sterile.	Negative.	Tuberculosis.
		....	Sterile.	....	Negative.	Sterile.	Negative.	Irregular febrile
		....	Sterile.	....	Negative.	Sterile.	Negative.	temperature.

NORMAL CASES—CULTURES TAKEN IN THE SECOND PERIOD ONLY.

Number.	First period: First to third day.		Second period: Fourth to seventh day.		Third period: Eighth to thirteenth day.		Remarks.
	Aerobic.	Anaerobic.	Microscopic.	Aerobic.	Anaerobic.	Microscopic.	
37	....	....	....	Sterile.	Sterile.	Negative.	Normal.
38	....	....	....	Sterile.	Sterile.	Negative.	Normal.
39	....	....	....	Sterile.	Sterile.	Negative.	Normal.
40	....	....	....	Sterile.	Sterile.	Negative.	Slight phlegmasia.
41	....	....	....	Sterile.	Sterile.	Negative.	Temperature once 101.20
42	....	....	....	Sterile.	Sterile.	Negative.	Normal.
43	....	....	....	Sterile.	Sterile.	Negative.	Normal.

NORMAL CASES—ERRORS IN TECHNIQUE WITH POSITIVE FINDINGS.

44	34	Mic. pyog. sur. Bac. xeroides. Mic. magna.	No obligat-ory anaerobe.	Gram posi-tive micro-cocci and bacilli.	See normal cases: Culture's taken in first, second, and third periods.					The first culture was taken as a demonstration. The tube became blocked and was accidentally withdrawn and vaginal secretion inspissated.
45	20	See normal cases: Culture's taken in first and third periods.	....	....	Mic. pyog. alb.	No obligat-ory anaerobe.	Gram posi-tive micro-cocci.			On last culture, tube was introduced without speculum. This growth considered vaginal or cervical contamination.
46	51	See normal cases: Culture's taken in first and third periods.	....	....	Mic. pyog. sur.	No obligat-ory anaerobe.	Gram posi-tive micro-cocci.			The last culture was taken by resident physician and mistake in technique was made.
47	24	Streptococcus, Bac. coli com.	No obligat-ory anaerobe.	Gram posi-tive micro-cocci. Gram negative bacilli.	....	....	....			Attempt to pass tube failing, it was withdrawn and passed by the aid of vaginal touch. Case normal clinically.
48	54	....	....	....	Mic. pyog. alb.	No obligat-ory anaerobe.	Gram posi-tive micro-cocci.			Tube boiled and passed without speculum.
49	55	....	....	....	Mic. pyog. alb. bac.	No obligat-ory anaerobe.	Gram posi-tive micro-cocci.			Tube passed without speculum; cervix not cleansed; cap opened in vagina.

ABNORMAL CASES OBSTETRICALLY—FORCEPS.

50	45	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	....	....	....	Low Sawyer forceps.
51	18	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	....	....	....	Simpson forceps. Slight fever on third day.
52	63	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Simpson forceps. Bad cervical tear. Much clotted blood in vagina at first examination. Vaginal discharge foul. Intra-uterine douche several times before last culture. Leukocytes, 14,000. Blood culture, negative.
53	40	Sterile.	Sterile.	Negative.	....	....	....	....	....	....	Low forceps. Temperature never febrile.
54	50	....	....	....	Sterile.	Sterile.	Negative.	....	....	....	Simpson forceps. Temperature never febrile.

ABNORMAL CASES OBSTETRICALLY—DOUCHES; MANUAL REMOVAL OF THE PLACENTA; VERSION; INTRA-UTERINE PACK

55	23	Sterile.	Sterile.	Negative.	....	....	....	Sterile.	Sterile.	Negative.	Temperature never febrile. Intra-uterine douche before culture.
56	17	Mic. alb.	No obligat-ory anaë-robe.	Gram posi-tive micro-cocci.	....	....	....	Sterile.	Sterile.	Negative.	Adherent placenta. Manual removal. Normal temperature.
57	35	....	....	....	Sterile.	Sterile.	Negative.	Sterile.	Sterile.	Negative.	Placenta previa with version. Gause pack. Irregular fever. Lechia foul. Complete tear. Child macerated. Blood culture negative.
58	46	....	....	....	Sterile.	Sterile.	Negative.	....	....	....	Intra-uterine pack.

ABNORMAL CASES OBSTETRICALLY—CRANIOTOMY.

59	30	Mic. pyog. alb., Bact. coli com.	No obliga-tory anaë-robe.	Gram posi-tive micro-cocci.	Mic. pyog. alb. Bact. coli com.	No obliga-tory anaë-robe.	Gram posi-tive micro-cocci.	....	....	....	Never febrile. Craniotomy. Fetid discharge. Probable muscular rupture of uterine wall.
60	11	....	....	Gram nega-tive bacilli.	Mic. mag-nus. Mic. pyog. aur.	No obliga-tory anaë-robe.	Gram posi-tive micro-cocci.	....	....	....	Craniotomy for hydrocephalus. Normal temperature.

## INTERCURRENT DISEASE—TYPHOID FEVER

Number.	First period: First to third day.			Second period: Fourth to seventh day.			Third period: Eighth to thirteenth day.			Remarks.
	Aërobic.	Anaërobic.	Microscopic.	Aërobic.	Anaërobic.	Microscopic.	Aërobic.	Anaërobic.	Microscopic.	
61	33	....	....	....	....	....	Sterile.	Sterile.	Negative.	Douche before admission. Blood culture. Bac. typhosus.

## GONORRHOEAL CASES.

62	12	Mic. pyog. aur.	No obligat- ory anaë- robe.	Gram posi- tive micro- cocci. Gonococci.	Mic. pyog. aur.	No obligat- ory anaë- robe.	Gram posi- tive micro- cocci. Gonococci.	....	....	Child developed ophthalmia neonatorum. Never febrile.
63	26	Sterile.	Sterile.	Gonococci.	....	....	Gonococci.	Sterile.	Gonococci.	Douche before second culture. Febrile after first culture. Diagnosis: Gonorrheal rheumatism and breast abscess.
64	67	Streptococcus.	No obligat- ory anaë- robe.	Gram posi- tive micro- cocci. Gonococci.	Sterile.	Sterile.	Negative.	....	....	Normal temperature.

## SEPTIC CASES.

65	3	Sterile.	Sterile.	Negative.	Streptococci	No obligat- ory anaë- robe.	Gram posi- tive micro- cocci.	....	....	Blood culture showed streptococcus pyogenes. Febrile third to fourteenth day. Breast congested. Many intrasternal discharges.
66	63	Streptococcus.	No obligat- ory anaë- robe.	Gram posi- tive micro- cocci. Gonococci.	Streptococci	No obligat- ory anaë- robe.	Gram posi- tive micro- cocci. Gonococci.	....	....	Febrile 3 days. Manual extraction of placenta. Puerperal discharge. Diagnosis: Puerperal pyemia.
67	21	....	....	....	....	....	Streptococcus.	....	Gram positive micrococci.	Blood culture: Streptococcus pyogenes.



To consider these 6 cases from the standpoint of actual the error occurring in each case:

CASE XXXIV.—The first culture showed *Micrococcus aureus* and *magnus* and *Bacillus xeroides*. The case was used for demonstration, the tube accidentally slipping, whereby vaginal secretion was inspired.

CASE XX.—First culture sterile; second culture gave *Micrococcus albus*. Here the variation consisted in the omission of the Sim's speculum in the introduction of the tube, it being guided into the cervix by the finger in the vagina.

CASE LI.—In this case the first culture was sterile, while the second, taken by an assistant, showed a growth, *Micrococcus aureus*. In both instances the variation in technique was identical, the vaginal speculum being omitted. From our knowledge of the ease of contamination, we consider that this second culture was contaminated by lack of care upon the part of a man inexperienced in the method. We admit that this contention is not proved.

CASE XXIV.—But one culture was made, and this gave the streptococcus and the colon bacillus. In this instance the Sim's speculum prevented sufficient depression of the tube to enable it to pass, so the former was discarded and the tube was passed by guidance of the finger. During the short time elapsing between the introductions, the tubes were both placed in the instrument tray, which was an additional source of possible infection.

CASE LIV.—Tube was introduced by guidance of a finger in the vagina. In addition, the tube was sterilized by boiling instead of by pressure.

CASE LV.—Tube was introduced, as in the last case, and, in addition, the cap of the metal tube opened while it was in the vagina during the introduction.

It is to be noticed that the omission of the Sim's speculum was noted in each instance in which in a normal case a growth was recorded. In two instances there were other factors present which would have been sufficient to cause contamination—in one case the protective cup was open during introduction, while in the other both tubes lay for several minutes in an instrument tray the sterility of which during that period must be considered doubtful.

Because of difficulties inherent to the work it was not possible, and, indeed, it did not seem desirable, to culture each case upon the same day of the puerperium, so we have divided the cultures into three periods. We have further divided the whole list of cases under various headings, as follows:

A. Clinically normal cases:

1. Cultures during first period (first to third day), 34 in number; all sterile.
2. Cultures during second period (fourth to seventh day), 29 in number; all sterile.

3. Cultures during the third period (eighth to thirteenth day), 18 in number; all sterile.

*B. Clinically normal cases with errors in technique and positive results:*

1. Cultures during first period, 2 in number.
2. Cultures during second period, 1 in number.
3. Cultures during third period, 3 in number.

(All of these cases, with one exception, in which but one culture was taken, showed negative results from other cultures made without error.)

*C. Clinically abnormal cases:*

(a) Forceps (in excavation or at outlet), 5 cases.

1. Cultures during first period, 4 in number; all sterile.
2. Cultures during second period, 3 in number; all sterile.
3. Cultures during third period, 1 in number; all sterile.

(b) Douches (intra-uterine), 1 case:

1. Cultures during first period, 1 in number; sterile.
2. Cultures during third period, 1 in number; sterile.

(c) Manual removal of placenta, 1 case.

1. Cultures during first period, 1 in number; growth.
2. Cultures during third period, 1 in number; sterile.

(d) Craniotomy, 2 cases:

1. Cultures during first period, 1 in number; growth.
2. Cultures during second period, 2 in number; growth.

(e) Version for placenta prævia (macerated foetus):

1. Cultures during second period, 1 in number; sterile.
2. Cultures during third period, 1 in number; sterile.

(f) Uterine packing:

1. Cultures during second period, 1 in number; sterile.

*D. Intercurrent disease:*

Typhoid fever (blood positive).

1. Cultures in third period, 1 in number; sterile.

*E. Gonorrhœa:*

1. Cultures during first period, 3 in number; all positive.
2. Cultures during second period, 2 in number; 1 positive.
3. Cultures during third period, 1 in number; positive.

One case, positive in the first and third periods, was unassociated with other organisms. In this case blood examinations were negative, but a mammary abscess and gonorrhoeal rheumatism were complications.

The second case, positive in the first and second periods, was associated with *Micrococcus aureus* in both cultures; while the third case, positive at the first culture and associated with streptococci, was negative in the second period and also sterile at this time.

*F. Septic cases (3):*

1. Cultures during first period, 2 in number; positive.
2. Cultures during second period, 2 in number; positive.
3. Cultures during third period, 1 in number; positive.

(Cultures not taken of third case during first or second period.)

Blood cultures were positive in 2 of the above cases, and were not taken in the third case.

#### GENERAL CONCLUSIONS.

1. The uterine lochia is sterile in normal cases throughout the puerperium.

2. Streptococci are never present within the cavum uteri without causing symptoms.

3. In a few instances non-pathogenic germs may be found in cultures in afebrile cases, but there is every reason to believe that their presence is really the result either of contamination during the extraction of the lochia or of their introduction during obstetric manipulation.

4. Ascendence of the gonococcus is an event of comparative rarity, though the frequency of this organism would of itself give reason to expect otherwise.

5. Infection of the endometrium is an ever present danger in culturing within a few days of delivery.

6. A study of the bacterial content of the puerperal uterus is of great importance as a subsidiary means of diagnosing septic infection following delivery.

7. As nearly as may be, a technique should be adopted which will prevent contamination during the removal of the lochia in order to avoid a vitiated result.

## REVIEWS.

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MODERN MEDICINE. ITS THEORY AND PRACTICE. In original contributions by American and foreign authors. Edited by WILLIAM OSLER, M.D., Regius Professor of Medicine in Oxford University, England. Assisted by THOMAS MCCREA, M.D., Associate Professor of Medicine and Clinical Therapeutics in Johns Hopkins University, Baltimore. In seven volumes. Volume III; pp. 960; 44 illustrations. Philadelphia and New York: Lea Brothers & Co., 1907.

VOLUME III of Osler's *Modern Medicine* is devoted to a consideration of those infections not dealt with in Volume II, as well as diseases of the respiratory tract. The most important subject discussed is tuberculosis, to which about 300 pages are devoted: E. R. Baldwin discusses the history and etiology; W. G. MacCallum, the pathology; and Lawrason Brown, the symptoms, diagnosis, prognosis, prophylaxis, and treatment. These contributions are of an unusually high order of merit; they comprise all of importance that is really known of the subject, and they reflect, on the one hand, the notable work done at Saranac under the inspiration and direction of Trudeau, and, on the other hand, the painstaking study of the pathology of disease at the Johns Hopkins University. Among the several topics of much interest dealt with by Baldwin are: the considerable reduction in the mortality rate of tuberculosis in civilized countries (from one-seventh of all deaths in 1890 to one-tenth of all deaths in 1900), a result attributable to the special attention given to the hygienic control of the disease; the different types of the tubercle bacillus—the human, the bovine, the avian, and the reptilian and piscine—and their points of similarity and means of identification; tuberculin; and the mechanism of resistance and immunity. MacCallum's article is a masterly description of the pathology of the divers lesions of tuberculosis. Of Brown's contributions, perhaps the section devoted to prophylaxis and treatment will be read with most interest by the general practitioner. Lack of space forbids detailed reference to the many important aspects of the question discussed, but the general breadth of view and wide scope of the article becomes apparent from a mere mention of certain of the subheadings, such as: State and municipal control of tuberculosis, trade regulations, general prophylaxis, individual prophylaxis.

laxis, and the many viewpoints from which treatment as such is approached: treatment at home and in institutions, the influence of climate, of hygiene, of diet, of medicines, of certain specific remedies, as well as surgery, and divers accessories. The article is altogether admirable and replete with many practical suggestions.

Dr. Osler, with the coöperation of John W. Churchman, provides an excellent discussion of syphilis, which well exemplifies a saying attributed to the Sage of Oxford (but then of Baltimore), that he who knows syphilis knows medicine. This chapter contains some interesting and well told historical data; an account of the etiological significance of *Spirochæta pallida*; an excellent description of the clinical manifestations of the infection in the different organs and tissues; a discussion of measures of prophylaxis, including some sane remarks upon the moot question of the state control of prostitution; and full details of treatment. Apropos of prophylaxis, the opinion is expressed that our greatest hope of controlling the ravages of the infection lies in educating not only the masses, but also the more educated classes, and that no one can accomplish more in this particular than the general practitioner.

Other contributions also deserve mention. The opening chapter in the book is on Malta fever, by Colonel David Bruce, whose name is indissolubly associated with the discovery of the specific etiological factor. The widespread prevalence of the infection is commented upon, and the evidence in support of the likely mode of infection by goat's milk is duly presented. Maximilian Herzog writes of beriberi, and discusses the many views entertained from time to time regarding its etiology. Among other matters he comments upon the results of the researches during the Russo-Japanese war, of Okata and Kobubo, who isolated a coccus that they believe to be the specific cause. Herzog was unable to confirm these results in about 50 cases studied in the Philippines, and, while professing his belief in the infectious nature of the disease, he inclines to the opinion that the specific cause has not yet been discovered. M. P. Ravenel discusses anthrax, rabies, and glanders, and among other interesting topics, points out the nature and the lesions of rabies, with the investigation of which in this country his name is well known; James M. Anders contributes a valuable study of tetanus, emphasizing the importance of using antitetanic serum in doubtful cases before the onset of trismus; Rufus I. Cole writes of gonococcic infections, of which not the least important are the metastatic phenomena (including the recently determined gonococcic nature of many cases of painful heel or painful foot), all of which are discussed in becoming detail; Isadore Dyer treats of leprosy, of which, perhaps, it suffices to say that it meets one's expectations; and Thomas R. Boggs, in a lucid manner, discusses a number of infections of doubtful nature, such as febricula, glandular fever, infec-

tious jaundice, miliary fever, Rocky Mountain spotted fever, psittacosis, foot-and-mouth disease, and milk sickness.

Three hundred and seventy-two pages are devoted to diseases of the respiratory tract, the contributions being as follows: The mechanics of respiration and of the respiratory tract, by Thomas R. Brown; diseases of the nasopharynx, pharynx, and tonsils, by Francis R. Packard; hay fever, by W. P. Dunbar; diseases of the larynx, by H. S. Birkett; diseases of the bronchi, by A. P. McPhedran; diseases of the lungs, by Hobart A. Hare; diseases of the pleura, by Frederick T. Lord; pneumothorax, by Walter B. James; and diseases of the mediastinum, by Henry A. Christian. In a series of articles of such uniform excellence, it is doubtless invidious to seek out any for special commendation; perhaps, however, without disparaging what remains, one may point to the excellence of Brown's contribution; of Dunbar's discussion of hay fever, in which he mentions his views regarding the etiology, as well as the results of his serum therapy; of McPhedran's description of bronchitis (following Marfan's classification); of Hare's treatment of bronchopneumonia; of Lord's discussion of pleuritis and its treatment; and of Christian's description of the intricate disorders of the mediastinum. James' article on pneumothorax, of a high order of merit, is much enhanced in value by several excellent colored illustrations. Packard's and Birkett's contributions are valuable articles by specialists for the general practitioner.

As a whole, the volume contains an unusual wealth of valuable information well presented; in general excellence, it is a worthy brother (or sister) of those that have gone before, and it augurs well for those that are to come.

A. K.

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**SURGERY, ITS PRINCIPLES AND PRACTICE**, by various authors.

Edited by WILLIAM WILLIAMS KEEN, M.D., LL.D., Emeritus Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College, Philadelphia. Vol. II, pp. 920; 572 illustrations. Vol. III, pp. 1132; 562 illustrations. Philadelphia and London: W. B. Saunders Co., 1907-1908.

THE second and third volumes of Keen's *Surgery* have followed with reasonable promptness the publication of Volume I, which was reviewed in these columns little more than a year ago. Volume II includes articles on diseases of bones, by Nichols, of Boston; fractures, by Eisendrath; surgery of joints, by Lovett and Nichols; dislocations, by Eisendrath; surgery of muscles, tendons, and bursæ, by Binnie; orthopedic surgery, by Lovett; surgery of the lymphatic system, by Gerrish; surgery of the skin, by John A. Fordyce, of New York; pathology of surgical disorders of the nervous system, by W. G. Spiller, of Philadelphia; surgery of the

nerves, by George Woolsey; traumatic neurasthenia, traumatic hysteria, and traumatic insanity, by F. X. Dercum; surgery among the insane, by J. Chalmers DaCosta; and surgery of the spine, by George Woolsey.

Among such a wide range of subjects, it will be impossible to select more than a few for comment. The surgery of the osseous system is well presented in the chapters by Nichols, Eisendrath, and Lovett; yet, in the treatment of the important subjects of fractures and dislocations, we must confess to disappointment. It is certainly simple, but it is scarcely satisfying, to be told that traumatic delirium is delirium tremens in non-alcoholics. The presentation of gunshot fractures is inadequate. In rupture of the main artery of a limb, Dr. Eisendrath advises immediate amputation. Perhaps at the present day it would not have been entirely out of place at least to suggest an attempt at arteriorrhaphy.

The classification of joint diseases adopted by Nichols, in describing their pathology, is not followed by Lovett in discussing the surgery of joints. The former adheres to a pathological classification rather than an etiological, because various causes produce identical lesions, and because the same cause at different times produces different lesions. The surgery of joints is discussed under the following heads: (1) Acute and chronic synovitis; (2) infective arthritis (gonorrhoeal, influenzal, typhoid, rheumatic, etc.); (3) arthritis deformans; and (4) tuberculosis. Lovett considers tuberculin unreliable for diagnosis; he gives the ultimate mortality for spine and hip tuberculosis as 30 per cent. If a cold abscess is very large, he advises that it be incised and cleansed, but neither packed nor sutured.

From the violence of the manipulations advised in the bloodless reduction of congenital dislocations of the hip, it is small wonder that Lovett states that "excessive extravasations are usual and temporary paralyses are not uncommon accompaniments of the operation." He reports 62.5 per cent. of anatomical repositions among 32 cases, secured by manipulation, at the Boston Children's Hospital. It would seem, on the other hand, that his strictures upon the dangers of instrumental force in correcting club-foot deformities argue either inexperience of these methods or unjustifiable force. The bibliography to the chapter on orthopedic surgery is very large, occupying two pages and a half, and apparently has been considerably reduced by the editors, a number of references in the text (Nos. 34 to 69, inclusive, for example) being wanting in the table of authorities cited.

The account of the surgery of the lymphatic system, by Gerrish, is admirable. He supports the view that it is a closed system. He maintains that Hodgkin's disease is an affection *sui generis*, neither tuberculous nor sarcomatous. There is included an exhaustive account of filariasis.

The surgery of the nervous system is admirably discussed by Spiller, Dercum, DaCosta, and Woolsey; but in the last article there is inserted an appalling list of *corrigenda*, which, alas! by no means includes all of the typographical errors. Spiller discountenances routine operation for fracture of the vertebrae; he advises against radical operation for glioma of the brain, holding decompression sufficient; he thinks gumma of the brain very unusual, stating that the lesion is much more apt to be meningitis or arteritis. Woolsey seems inclined to accept the theory of peripheral regeneration of axones. DaCosta, in discussing craniotomy for microcephalus, says with characteristic force that "the surgeon who removes a strip of the skull in order to cause the brain to develop acts as wisely as would a man in removing a section from the dome of a cathedral in order to increase the stature of the archbishop."

Volume III opens with an article on the surgery of the head, by Harvey Cushing. There follow chapters on the surgery of the neck, by E. Wyllys Andrews, of Chicago; on diseases of the thyroid gland, by Dr. Albert Kocher; on the nose and its accessory sinuses, by Harmon Smith, of New York; the larynx, the trachea, and the thorax, by George E. Brewer, of New York; surgery of the breast, by Finney; of the mouth, teeth, and jaws, by Edmund Owen; of the tongue, by Da Costa; on the technique of abdominal surgery, the surgery of the abdominal wall, of the retroperitoneal space, and of the peritoneum, by John C. Munro, of Boston; surgery of the œsophagus, by Professor Gottstein, of Breslau; of the stomach, by Mayo Robson; of the liver, gall-bladder, and the biliary ducts, by William J. and Charles H. Mayo; and on the pancreas and spleen, by Moynihan.

The most valuable as well as the longest (260 pages) of these articles is that by Cushing, on the surgery of the head. It fully justifies for itself the claim made by the publishers for all the articles, namely, that of being a complete monograph on the subject discussed. The article is encyclopedic; we have noticed no faults of omission, and if there be any fault of commission, it is, perhaps, shown in the tendency to regard the operation described as "sub-temporal decompression" as a panacea. The account of the mechanism of skull fractures is illuminating. Cushing deprecates search for the bullet in gunshot wounds; he urges the operative treatment of hemorrhages in the new born; he prefers ligation of the carotid to ligation of the orbital veins for pulsating exophthalmos; he advises postponing exploration for brain abscess until a day or two after cleaning out the mastoid, to see whether the symptoms subside; he repeatedly warns against the danger of indiscriminate lumbar puncture; and he regards as useless the time-honored practice of venesection for cerebral compression, because high blood pressure is the result, not the cause, of the condition. He thinks craniocerebral topography overestimated, because it is never



entirely accurate; he prefers to class as endotheliomas tumors commonly known as fibrosarcomas; he insists on the difficulty which sometimes exists in differentiating the cerebral symptoms of nephritis from those of brain tumor; and he states that apoplexy in the young is not infrequently due to hemorrhagé into a tumor in a silent region of the brain. He never uses the dental engine, preferring hand-driven instruments.

The article on the surgery of the neck is carelessly written, and the appended bibliography is a mere jumble of titles, useless, because no references to them are to be found in the text.

Dr. Kocher writes that "the function of the parathyroids is partly, or perhaps chiefly, to take up the toxic or secretory materials of the thyroid gland and to prepare them for more rapid excretion through the kidneys." He states of surgical treatment of Graves' disease that "to say that this is still the best is not enough." But it must be acknowledged that this dictum is based on empiricism rather than on pathology, and that it is liable to be questioned so soon as the pathology of the disease shall be thoroughly understood. Prof. Kocher's 200 operations for Graves' disease gave an operative mortality of 4.5 per cent., with 85 per cent. of cures.

Apart from a rather overcolored picture which he draws of the advantages of Sauerbruch's air chamber, there is nothing particularly noteworthy in Dr. Brewer's chapter on thoracic surgery. Finney gives a good account of Paget's disease of the nipple, and insists on its malignancy; but his descriptions of tumors of the breast lack definiteness.

Owen contributes an excellent article on surgical affections of the mouth, teeth, and jaws. He cadidly says that patients with epithelioma of the mouth usually come to the surgeon in such a condition that if he considered only his own peace of mind he would decline to interfere. DaCosta, writing on the surgery of the tongue, insists on the removal of the lymph nodes, even in the "earliest" cases, stating that they are always microscopically invaded, and that if the base of the tongue is involved, both sides of the neck are infected.

Munro's articles on the abdomen, while excellent, present nothing calling for special comment. It may be thought that he aimed to condemn with faint praise Ochsner's treatment of peritonitis. He gives no satisfactory idea of the prognosis in cases of diffuse peritonitis under any form of treatment.

Robson urges gastro-enterostomy for ulcer of the stomach, even if the ulcer be excised. He advises free irrigation in "general septic peritonitis" from perforation, and also urges gastro-enterostomy after suture of the perforation if the patient can bear it. The Mayo brothers minimize the functional value of the gall-bladder; they have removed it in one out of every three patients. The article is particularly good in description of operative detail, but leaves something to be desired in regard to the pathogenesis of

these diseases. Moynihan's chapters on the pancreas and spleen are characterized by their comprehensiveness, and by the author's usual clearness of diction.

As a whole, the several chapters furnish their readers with a representative account of modern surgery, in which practice decidedly overshadows principle, but which, in a few instances, include enough of the latter to render them absolutely authoritative.

A. P. C. A.

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**PULMONARY TUBERCULOSIS: ITS MODERN AND SPECIALIZED TREATMENT.** By ALBERT PHILIP FRANCINE, A.M., M.D. Second edition. Philadelphia and London: J. B. Lippincott Company, 1907.

ALTHOUGH much has been written on the modern treatment of pulmonary tuberculosis and the remarkable results that have been obtained, the vast majority of the medical profession have not yet acquired a sufficient knowledge of the hygienic method to carry it out successfully. There is truth in the somewhat paradoxical statement that the general practitioner should be a specialist in phthisiotherapy. He is the man behind the gun in the fight against tuberculosis, as Dr. Osler has said, and if the fight is to be a winning one, the general practitioner must do effective work. The present volume forms a trustworthy guide to the hygienic-dietetic treatment of this disease. The different aspects of the subject are presented in a clear and interesting manner. A good deal of valuable information has been collected that will not be found in larger and more pretentious works. The chapters on rest, diet, and climate are excellent. The great importance of rest is emphasized, and the statement of Hilleary is endorsed that "exercise brings more tuberculous patients to grief than all other things combined." The position held in regard to the vexed question of climate is the "golden middle road" between those who deny altogether its influence and the other extremists who hold, with the committee of the National Association, that in those cases treated by change of climate the amelioration of symptoms and general improvement "far surpass the very best results obtainable in similar advanced cases in our cities on porches or roof gardens."

It is to be regretted that the diagnostic use of tuberculin is not more fully described, and also the method of preparing the proper dilution for injection. The only dosage given is that of Pickert, who begins with 0.5 mg. and whose maximum does is 2.5 mg. of old tuberculin. Koch's original procedure, with an initial dose of 0.1 or 1 mg. and a maximum of 10 mg., certainly deserves mention. It is still in general use, and is the one recommended with minor modifi-

cations by a number of the most recent writers (Bendelier, Junker, Roepke). A maximum dose of 5 mg. is advised by Turban, while Cornet, B. Fraenkel, Schlüter, Madison, and others insist on the importance of employing a final dose of 7 or 10 mg. if a negative result is obtained with smaller amounts. The statement is made on the authority of Roth-Schulz that a rise in temperature of  $0.1^{\circ}$  F. above the previous maximum is considered a positive reaction. This is an unfortunate typographical error. In the paper quoted Roth-Schulz says the increase should be at least  $0.5^{\circ}$  C. Dr. C. L. Minor's admirable "Hints and Helps" to tuberculous patients are included in the volume.

J. H. P.

ETUDE HISTO-CHIMIQUE ET CYTOLOGIQUE DE CRACHATS. Par LE DR. S. ISRAELS, de cong, ancien interne lauréat des Hopitaux de Paris, Pp. 151. 4 plates. Paris: G. Steinheil, 1907.

THE monograph is confined exclusively to an elaborate micro-chemical and cytological study of the sputum, instigated by the work of Bezeron and others upon the cytodagnosis of body fluids. For this investigation special stains, particularly the polychrome methylene blue of Unna were used. The author by his methods differentiates true mucus both from a reticulated mucus which is derived from degenerated cells, and from a sero-albuminous exudate which in its micro-chemical reactions resembles the albuminous fluid of a pleural exudate. True fibrin was not seen in the sputum. The cytological study of the sputum in different diseases did not bring out any very new facts, though certain interesting changes in the cell-content of the sputum, during such diseases as pneumonia, could be followed.

W. T. L.

MATERNITY. By HENRY D. FRY, M.D., Sc.D., Professor of Obstetrics in the Georgetown University, Washington, D. C. Pp. 220. New York and Washington: The Neale Publishing Co., 1907.

WE must admit that our first feeling is always one of hostility to books which aim at the medical instruction of the laity. We believe that the majority which have appeared had better not have been written, and that much harm has been done by such publications. With these convictions, it will readily be understood that we approached this volume with anything but pleasurable expectations, particularly as it is our pet conviction that the less a woman knows

of the possibilities of labor and pregnancy, the better it is for her peace of mind. We are glad, however, to be able to give the book our approval. Its advice is sane and in accord with what we are pleased to consider the best teachings of the day. It opens with an exceedingly interesting historical sketch of childbearing, followed by a chapter upon the hygiene of girlhood. The various subjects relative to the childbearing process are discussed, and the book ends with chapters upon the care and feeding of infants.

The author writes from a rich experience both as a teacher and practising obstetrician, an advantage which, we are compelled to say, is but rarely possessed by those preparing books for lay readers. The book can be safely placed in the hands of the pregnant woman; moreover, a mastery of its contents will tend to advance the cause of scientific care during this period, since women would be in a position to demand better oversight than is received by the large majority even at the present day.

W. R. N.

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**SURGICAL INSTRUMENTS IN GREEK AND ROMAN TIMES.** BY JOHN STEWART MILNE, M.A., M.D. (Aberd.), Keith Gold Medalist in Clinical Surgery. Pp. 187; 54 plates. The Clarendon Press, Oxford, England, 1907.

THIS book, which was presented as a thesis in an examination for the degree in medicine in the University of Aberdeen, endeavors to give an account of the various instruments used by the medical profession in ancient Greece and Rome. The material used was gathered from various museums, especially those of Europe, and a patient and no doubt laborious search in the literature of a half-dozen languages. Such industry deserved the "Highest Honors" gained, and has resulted in a worthy addition to the too scanty literature in English of the work of our predecessors. The author discusses the material, execution, and ornamentation of various instruments, and describes the types of knives, probes, forceps, cauteries, etc., which were used. Among the many interesting facts contained in the volume may be mentioned the use of a varix extractor by Galen, an instrument which in recent years has been rediscovered; a lenticular or chisel guarded by a button and driven by a hammer through the skull to form an osteoplastic flap; the use of the uterine sound by Hippocrates for correcting malpositions of the uterus and for dilating the cervix, which instrument was subsequently rediscovered by Simpson.

The volume is completed by the insertion of 54 plates, reproducing from photographs a great variety of instruments stored in various museums.

G. P. M.

NOTHNAGEL'S ENCYCLOPEDIA OF PRACTICAL MEDICINE. DISEASES OF THE HEART. By PROF. TH. VON JURGENSEN, of Tübingen; PROF. DR. L. KREHL, of Greifswald; and PROF. DR. L. VON SCHRÖTTER, of Vienna. Edited, with additions, by GEORGE DOCK, M.D., Professor of Medicine in the University of Michigan, Ann Arbor. Authorized translation from the German, under the editorial supervision of ALFRED STENGEL, M.D., Professor of Clinical Medicine in the University of Pennsylvania. Pp. 848; 81 illustrations. Philadelphia and London: W. B. Saunders Co., 1907.

THE volume of Nothnagel's *Encyclopedia* devoted to Diseases of the Heart is so well and favorably known even to those that have only a nodding acquaintance with German, that it suffices perhaps merely to mention the publication of an English translation. Professor von Jürgensen discusses insufficiency (weakness) of the heart, endocarditis, and valvular disease; Professor Krehl, diseases of the myocardium and of the nervous mechanism of the heart; and Professor von Schrötter, diseases of the pericardium. If there is some overlapping and some repetition—almost if not quite inseparable from collaborated books—this is, as the editor points out, “more than made up by finding in the book the sound learning and wide clinical experience of Professors von Jürgensen and von Schrötter, and the deep and broad training in anatomy, physiology, and pathology, as well as the excellent clinical observation, of Professor Krehl.” While Dr. Dock has not attempted radical alterations or additions, he has materially enhanced the value of the book by incorporating important contributions, chiefly American and English, that have appeared since the volume was originally published in German.

A. K.

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DISEASES OF THE MALE GENERATIVE ORGANS. By EDRED M. CORNER, M.A., M.B., B.Sc., M.C., F.R.C.S., Surgeon to Out-Patients, St. Thomas' Hospital, London. Pp. 279; 41 illustrations. London: Henry Frowde, Oxford University Press; Hodder & Stoughton, 1907.

It is with considerable surprise that one learns that so much can be written upon this subject after the author has excluded the following topics: gonorrhœa and syphilis; affections of the prostate; and all diseases of the urinary tract. Thus pared down, the topics discussed at somewhat tedious length in this volume are: hydroceles and hematoceles; physiology of the testicle; the wandering or movable testicle; the imperfectly descended testicle; the testicle, its

relation to its blood supply, its duct, and inflammation; torsion of the testicle; epididymitis, orchitis, etc.; functional affections; diseases of the spermatic cord and of the vesiculæ seminales; some diseases of the urethra; diseases of the prepuce and penis, and of the scrotum.

Much of the matter contained in this book has been published by the author from time to time in somewhat similar form, in various journals; but the subjects are greatly elaborated in their present dress, and may prove of interest to those who do much pediatric surgery. Particularly instructive are Mr. Corner's well-known studies of the wandering testicle, and its relation to hernia in childhood; also the sections dealing with tuberculosis of the testicle.

A. P. C. A.

**MANUAL OF ANATOMY, SYSTEMATIC AND PRACTICAL, INCLUDING EMBRYOLOGY.** By A. M. BUCHANAN, M.A., M.D., C.M., F.F.P.S. (Glas.), Professor of Anatomy in Anderson's College, Glasgow, Scotland. Vol. II; pp. 965; 363 illustrations. Chicago: W. T. Keener & Co., 1907.

VOLUME II, of Buchanan's Anatomy is devoted to the abdomen, the thorax, the head and neck, the nervous system, and the organs of special sense. It follows the general plan of Volume I, which we have already noticed. At the end of the different sections are directions for dissecting; those relating to the abdomen and the thorax are excellent. The illustrations—line cuts, in black and colors—are mostly original and good. An appendix contains the Basel anatomical nomenclature and a useful glossary. As we said of Volume I, the book is a personal work, reflecting the views of a distinguished teacher, and, doubtless, it will be well received and prized by the author's students and friends; but lacking any features that distinguish it in a noteworthy manner from other good anatomies, it probably will not appeal to a very large circle of readers.

A. K.

**ELEMENTS OF HUMAN PHYSIOLOGY.** By ERNEST H. STARLING, M.D. (Lond.), F.R.C.P., F.R.S., Jodrell Professor of Physiology, University College, London. Eighth edition; pp. 716; 323 illustrations. Chicago: W. T. Keener & Co., 1907.

THAT a book reach the eighth edition it must be meritorious; that Professor Starling's *Elements of Human Physiology* is meritorious is known to all who take any interest in the subject. Professor Starling has aimed to give in the shortest possible compass the essentials of physiology that should be familiar to every student and practitioner, and he has succeeded well. The book, undoubtedly, will secure an ever increasing circle of readers.

A. K.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**The Passage of Pancreatic and Intestinal Juices and of Bile into the Stomach.**—BOLDYREFF (*Zentralbl. f. d. med. Wissensch.*, 1908, xlv, 194; *Pflüger's Archiv*, cxxi, 13) has made a complete review of the literature concerning this question before giving the results of his own observations. His work was done upon dogs in which a gastric fistula had been produced. Boldyreff found that there was a passage of pancreatic and intestinal juices and of bile into the stomach, and that this occurred under definite conditions, the result, apparently, of physiological demands. This passage occurs not occasionally as a result of antiperistalsis, but constantly when the proper conditions exist. The physiological causes of the entrance of duodenal contents into the stomach are the following: (1) The placing of fat in the empty stomach; (2) the feeding of fat-rich food; (3) the presence of large quantities of hydrochloric acid in the stomach, whether at the height of digestion or from secretion of acid into the empty stomach; and (4) the presence of other acids in the stomach, such as lactic, acetic, butyric. Occasionally no cause was demonstrable. The addition of the duodenal secretions led to a destruction of the pepsin, since the gastric contents no longer showed digestion of proteins after they had been rendered acid. In a dog whose stomach was shut off from the duodenum, no digestion of fat took place. Boldyreff was able to show on himself and another person by passage of the stomach tube after taking 80 to 100 grams of oil, that the pancreatic juice had passed into the stomach. This procedure may be of use in obtaining pancreatic juice for diagnostic purposes. The observations show that after ingestion of considerable fat the digestion in the stomach is performed mainly by the pancreatic ferments, and further, that in healthy adults one need not expect to find pepsin or hydrochloric acid in the gastric contents, if there has been an admixture of intestinal juice.

**A New Method for the Quantitative Determination of Pepsin.**—SOLMS (*Deut. Arch. f. klin. Med.*, 1907, lxiv, 159) believes that the method he has devised is the most accurate yet proposed for the quantitative estimation of pepsin. Two solutions are required: (1)  $\frac{N}{10}$  hydrochloric acid, and (2) 1 per cent. solution of ricin in a 5 per cent. aqueous solution of NaCl. Solution 2 is filtered; the filtrate is slightly turbid and becomes milky on the addition of the decinormal acid. Pepsin is capable of rendering clear a turbid ricin solution. The technique is as follows: The gastric contents are removed an hour after the Ewald test breakfast, as usual. The free hydrochloric acid, if present, is then determined quantitatively, likewise the total acidity. The gastric juice is now diluted, according to the degree of the acidity (the total acidity is taken as a guide, 40 to 60 being considered normal). With normal acidity the gastric juice is diluted 1 to 100 (to 1 to 1000); with hyperacidity 1 to 100 (to 1 to 10,000); with anacidity or marked subacidity 1 to 10 (to 1 to 100). For the sake of clearness the following examples may be quoted: With a graduated pipette 2 c.c. of the filtered ricin solution is placed in each of five test-tubes. With a second pipette 0.5 gram of decinormal HCl is added to each of these tubes, rendering the fluid very turbid. Now one adds to the first tube 1 c.c. of boiled gastric juice (ferment destroyed), to the second tube 0.9 c.c., to the third 0.8 c.c., to the fourth 0.5 c.c., and to the fifth 0 c.c. Then take the diluted gastric juice whose pepsin content is to be determined (1 to 100 dilution for normal juice) and to the first tube (containing the ricin solution, tenth normal acid, and boiled gastric juice) add 0 c.c. of it, to the second 0.1 c.c., to the third 0.2 c.c., to the fourth 0.5 c.c. and to the fifth 1.0 c.c. Thus, each test-tube contains about 3.5 c.c. of fluid. The tubes are stoppered and placed in the incubator for three hours, or at room temperature for a longer time, when they are examined; observe which of the tubes contains a clear fluid. For purposes of convenience Solms says that a gastric juice has 100 pepsin units when 1 c.c. of a 1 to 100 dilution of the juice clears the ricin solution after three hours in the incubator. In examining normal gastric juices, as judged by the acidity values, the author finds that 100 pepsin units is a normal quantity of pepsin, although with normal acidities he has obtained as much as 200 to 500 pepsin units. With anacidity and low total acidity the pepsin values were constantly low, about 10 to 20 units or less. Hyperacidity, on the other hand, does not usually show a corresponding increase in the amount of pepsin, the amount being normal generally. Thus far the author can see no aid in a diagnostic or therapeutic way to be obtained from the quantitative determination of the pepsin in the gastric contents. The method apparently marks a distinct advance in simplicity and accuracy.

**Banti's Disease, with Report of Two Cases.**—W. OETTINGER and N. FIESSINGER (*Revue de méd.*, 1907, xxvii, 1109) state that since Banti first described the condition named after him, about thirteen years ago, despite the interest which has been shown in it, the pathogenesis has remained somewhat obscure. Some have thought that the process arose first in the liver and subsequently affected the spleen, while others assert that the spleen is first affected, and by its close connection with the



liver by means of the portal system may transfer easily the pathological cause to that organ. It is naturally important to settle this question. If the spleen be the point of origin, splenectomy might be expected to arrest the process. In the two cases reported by Oettinger and Fiessinger this previous involvement of the spleen before alteration of the liver was definitely made out. Pathologically, the liver showed no cirrhosis beyond some sclerosis surrounding the portal veins; the hepatic veins, the biliary system, and the hepatic arteries were normal. The splenic vein from its entrance into the portal system and toward the spleen showed a marked endophlebitis, whereas the rest of the portal system, especially the mesenteric portion, was apparently normal. The spleen itself in both instances was markedly altered, and showed much sclerosis of the normal soft, pulpy portion. This change in the spleen has been shown to be due to a hemolytic process, the cause of which is not noted by Oettinger and Fiessinger; they conclude, however, from their study that these hemolytic poisons travel along the splenoportal system, as shown by the endophlebitis, and ultimately the liver is affected. These facts, they say, indicate the need of early surgical interference; splenectomy, especially in the early slow development of the disease, offers the only chance for a cure.

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**The Presence of Spirochetes in Pseudoleukemia, Acute Lymphatic Leukemia, and Lymphosarcoma.**—W. E. WHITE and F. PROESCHER (*New York Med. Jour.*, 1908, lxxxvii, 9), having previously found spirochetes in the glands of pseudoleukemia and also in the fluid aspirated from the glands in a case of acute lymphatic leukemia, were led to work along these lines, and this study is based on fourteen cases of the above diseases, from the glands of which, whether removed from living patients or obtained at autopsy, similar spirochetes were found. From one of the lymphosarcoma cases White and Proescher were able to transfer a purely glandular affection to a guinea-pig by a subcutaneous inoculation from one of the sarcomatous glands. This they have transferred through four generations of animals, recovering in each the same organism. The spirochete differs from those previously described in its great length and the shallowness of the curves of its body, and may be seen in the freshly expressed juice of the glands or in sections stained by Levaditi's method, or in smears following the method of Proescher. White and Proescher give the name *Spirochaeta lymphatica* to the organism, but say further study is necessary before its relation to the disease can be definitely proved. However, they have never been able to find it in normal or tuberculous glands and the fact of finding these organisms in the different members of this more or less closely allied group of diseases, and the ability to transfer one type of it to four generations of guinea-pigs and recover the organism in each case, have led White and Proescher to suggest the following classification of this disease based upon this supposed etiology: Lymphatic spirillosis: Acute form—(a) with lymphocytosis, and (b) without lymphocytosis; chronic form—(a) benign, without sarcomatous change or with sarcomatous change, and (b) malign, with sarcomatous change or without sarcomatous change.

**Gumma of the Heart.**—H. HUCHARD and NOEL FIESSINGER (*Revue de méd.*, 1907, xxvii, 948), on account of the lack of definite symptoms and obscurities in diagnosis of gumma of the heart, give a most careful review of the literature on the subject and report in detail a case of their own. The first reported case in the literature dates back to 1775, and subsequently many others have been reported. They are briefly summarized by Huchard and Fiessinger who note the following points: As regards etiology, males are more commonly affected than females—about 60 per cent. of 47 cases. Twenty-two of these occurred between the ages of thirty-one and forty years; the left ventricle was most commonly affected. As regards the clinical manifestations of the trouble, Huchard and Fiessinger point to no definite syndrome, but note the importance, in old syphilitics, of a history of gradually progressive dyspnoea, oedema, and cyanosis. The pulse is often small, rapid, of high tension, and at times irregular. The heart and liver may be enlarged and albuminuria and polyuria present. The gummas are so often latent, however, that few symptoms develop until sudden death occurs and the diagnosis is made at autopsy. In concluding, Huchard and Fiessinger report several cases from the literature in which cardiac conditions developing in luetic patients have been either cured or greatly improved by specific treatment associated with very little cardiac therapy, and say that this is the best proof of the diagnosis of a syphilitic cardiac affection, whether gummatous or otherwise, and that a specific form of treatment, in doubtful cases, may even help some non-luetic affections, while in the positive cases a cure which could never be reached by ordinary cardiac treatment, is attained.

**Experimental Syphilis.**—ELIE METCHNIKOFF (*Revue de méd.*, 1907, xxvii, 952) reviews the experimental work that has been done up to the present time on the higher apes and other animals, and the more modern methods for diagnosis. As regards prophylaxis, the use of serums, vaccines, and other things being so unsatisfactory, the author and M. Roux were led to experiment with an ointment having a mercurial base, which was found, if applied within eighteen hours after inoculation, to prevent the infection without, however, conferring any immunity against future inoculation. Of the many preparations used, the best was found to be 25 to 33 per cent. calomel, with from 75 to 67 per cent. of lanolin. After many successful experiments on animals, a final test was made with the consent of a young doctor, who, one hour after inoculation with a syphilitic virus was treated with a calomel ointment (25 per cent.), and after one year has shown absolutely no signs of any luetic disease. Metchnikoff hopes that the systematic use of this calomel ointment may reduce the great frequency of this dread disease. As regards treatment, Metchnikoff speaks of mercurial injections and also of the lately advocated use of the arsenical preparation (atoxyl), which, it may be hoped, will in future give better results.

**Renal Complications and Sequels of Influenza.**—H. STERN (*Medical Record*, 1908, lxxii, 46) notes that there is a lack of consideration paid to the renal troubles that may be traced to influenza, possibly owing to their slight character at first or the lack of care bestowed upon the patient

after the more prominent phenomena of influenza have subsided. Stern distinguishes three forms of complications: (1) Cases with acute symptoms of renal involvement; (2) cases in which there occurs an aggravation of a preëxisting renal disease; and (3) postinfluenzal nephritis. As regards the first group, there may be simply the usual febrile congestion, such as may accompany any acute infectious disease which rapidly clears up after convalescence, but in a few cases, about 2 to 4 per cent., there may be an acute nephritis of a more or less severe type due directly to the influenza. The second variety is of decided importance as regards prognosis, especially as influenza may light up a latent nephritis, which has previously shown few or no symptoms, into a much more serious and even fatal process. The third class is of importance, especially in those cases of influenza with a long protracted convalescence; it is in this class that subsequently the signs and symptoms of renal inefficiency gradually develop. Thus, of 14 cases of protracted convalescence and general systemic decline after an attack of influenza, that were examined by the author, in from three to ten weeks after the attack, 7 showed some impairment of renal function, and 2 others definite renal disease.

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**Alimentary Poisons and Atheroma.**—M. LOEPER (*Arch. d. maladies du cœur, des vaisseaux, et du sang*, 1908, i, 45) asserts that various organic lesions have their origin in the digestive tract, toxic products being absorbed; the cardiovascular system may be among the first to suffer from the irritant action of such poisons. He divides the alimentary intoxications into four classes: those which result from the direct poison of certain foodstuffs; those which result from their alteration and change; those arising from their putrefaction; and finally, those which result from the ultimate destruction of certain nutritive products in the tissues. The first class may come from some of the vegetables, fishes, ordinary meats, and drink; the second, from game, sweetmeats, and fowl; the third, from products of intestinal putrefaction; and the fourth from the bodily excretions, as lactic acid, uric acid, and perhaps also creatin and creatinin. Loeper's experiments with these different substances were made on rabbits with a resulting sclerosis of more or less severe degree (this is illustrated in plates), and although Loeper says the doses of these poisons may have been larger and more severe in animals than in man, yet the repeated absorption in the human being of minute doses of these poisons will result in the same condition. Knowing this to be so, he concludes that, either in health or disease, the prescription of certain diets or the forbidding of foodstuffs giving rise to the above-mentioned products may prevent or at least alleviate an arteriosclerosis that might progressively increase, an "atoxic regime" being, of course, the ideal, which, however, is hard to attain.

Along these same lines another article is that on "experimental work arteriosclerosis," by OSCAR KLOTZ (*Montreal Medical Journal*, 1908, xxxvii, 16), who notes the factor of work and increased arterial pressure on the arteries in producing sclerosis. It has been noted clinically in the adult that vessels of the more active organs show hypertrophy and sclerosis earlier than in the less active parts. In right-handed persons the radials on that side are considerably more sclerosed than on

the left, and the reverse is true in left-handed persons. The same is true for those who walk much or are on their feet frequently, the most advanced arterial changes in these persons being in the vessels of the legs. These facts all point to the prominent part played by work in arteriosclerosis. To find out whether this factor of work alone unaided by toxic agents could produce sclerotic changes, the author experimented on healthy nine-months-old rabbits by suspending them by their hind legs for a few minutes a day over a long period of time, thus causing not only increased work, but also, by the inverted position, considerable increase in pressure in the thoracic aorta above the normal, and this without the aid of drugs. At autopsy macroscopical and microscopical changes could easily be made out in the aorta and its branches above the renal vessels. There were two kinds of changes noted in the vessels, one in the intima alone, and the other in the media. In the latter type degenerative changes occur and fusiform aneurysms are formed. Klotz concludes that from these experiments work plays a very important role in the production of arteriosclerosis of different character; that even in vessels of different histological structure sclerotic changes can be brought out by increased work; and further, that as a consequence of certain changes, degenerative in character, taking place as the result of increased work in the media of the vessels, aneurysms may result.

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## SURGERY.

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UNDER THE CHARGE OF

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**A Contribution to the Study of Jejunostomy.**—DELORE and THEVENOT (*Archiv gén. d. chir.*, 1908, ii, 237) say that jejunostomy does not merit the discredit into which it has fallen, in the view of many surgeons. The results are good when a simple technique is employed. Preference is given to two methods of operation: the one proposed by Drucbert in which a canal is made leading out from the intestine between the serous and the muscular coats of the intestine; the other proposed by Eiselberg and Witzel in which the canal is made along the wall of the intestine by plicating it over a catheter as in the similar method of performing a gastrostomy. The chief object of any method is to obtain an opening in the bowel which will be continent. It should be one that can be easily and rapidly made and one that may be only temporary.

More complicated operations do not accomplish more than these simple ones and are not tolerated as well by the enfeebled patients. Jejunostomy is indicated: in cancer of the œsophagus when the stomach is so retracted that one cannot do a gastrostomy; in cancer of the stomach when the situation and extent of the lesions will not permit a gastrostomy or a gastro-enterostomy, and when under any circumstances in such cases a gastrostomy is impossible; in gastric fistulæ, spontaneous or surgical, when the orifice cannot be closed by direct sutures and is situated in the pyloric region. In burns of the stomach by corrosive fluids, jejunostomy is the only convenient immediate treatment for the diffuse lesions. It is indicated when active ulcers cannot be removed or are complicated by acute or chronic hemorrhages, rebellious to medical treatment. Gastro-enterostomy is preferable when the ulcer is located in the pyloric region and is accompanied by stenosis of the pylorus. Jejunostomy has a physiological basis. It assures complete rest of the stomach and is indicated whenever rest is necessary for the cure of lesions of this organ.

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**Simultaneous Radical Operation on a Femoral and an Inguinal Hernia on the same side.**—BERNDT (*Zentralbl. f. Chir.*, 1908, xxxv, 393) made an incision parallel to and immediately over Poupart's ligament, divided the external oblique from the external ring outward, isolated, ligated, and removed both the sacs of the femoral and inguinal herniæ. The spermatic cord was then lifted and the internal oblique muscle together with the transversalis were brought downward until they were visible under Poupart's ligament, when the horizontal ramus of the pubis could also be seen. A curved needle with a silk suture was then passed through the lower edge of the internal oblique and transversalis muscles, then through the periosteum of the pubic bone until the needle appeared external to the femoral canal. The other end of the suture was then passed through the lower edge of Poupart's ligament. Both ends were then caught in a hemostat. Two or three similar sutures were then introduced and all tied thus closing the femoral canal. About three more sutures were introduced according to the Basini method, to bring the internal oblique and transversalis to the lower edge of Poupart's ligament. The spermatic cord was then laid in position and the external oblique sutured over it in the usual manner.

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**Conservative Operations upon Sarcomas of the Long Bones.**—BORCHARD (*Deut. Ztschr. f. Chir.*, 1908, xciii, 1) says that in cases of sarcoma originating in the bone or periosteum of the long bones, conservative methods of operation should receive the most consideration. It is not the microscopic picture, but the macroscopic, that is, the extent of involvement, which will decide whether or not a conservative method of treatment is to be employed. In all encapsulated tumors it is the operation of choice, and even in moderate sized, so called, infiltrative tumors it should be employed. Only when the soft parts are so extensively involved in the growth, or a part necessary to the preservation of the extremity, should the mutilating operations, excision and amputation, be considered. In the treatment of the more malignant tumors

the performance of conservative operations should be the rule, that of the mutilating operations the exception. Functional failures are not to be much feared, since the muscles can adapt themselves to extensive shortening of the bones, and since the ability of the bones to regenerate may be delayed and later go on to completion with resulting firm union. The age of the patient is not very important. In suitable cases plastic operations should be done. The simple removal of the tumor is to be permitted only when it is completely surrounded by good bone and when this remaining surrounding bone is sufficient to guarantee the firmness of the limb, or when a companion bone will supply the deficiency. A removal of a part of a joint surface will be permitted, since this can be replaced by a plastic operation. By a sufficiently extensive resection into the sound tissues, by the employment of the plastic operations at our command, and by sufficient patience, we may obtain results, which as far as their permanency and functional effect is concerned, will be far better than those to be obtained from the mutilating operations. More patients will be saved because they will undergo these operations earlier than amputations or excisions.

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**The Treatment of Gonorrhœal Arthritis of Large Joints by Means of Passive Hyperemia.**—BAETZNER (*Deut. Ztschr. f. Chir.*, 1908, xciii, 46) says that the treatment by passive hyperemia has established an important advance in the therapy of gonorrhœal arthritis. The relief from pain afforded by it is marked. The clinical course of the disease becomes considerably milder under its influence. It permits more early movement of the joint. The duration of the disease is considerably shortened and the functional results improved. Ankylosis was not observed in any of Baetzner's cases. The treatment is simple, technically not difficult, and its cheapness makes it accessible to many cases. Baetzner believes, on the basis of his cases, that passive hyperemia should be extensively employed in the treatment of gonorrhœal arthritis.

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**Apropos of Total Extirpation of the Urinary Bladder.**—GRAEUWE (*Jour. de chir., et. ann. d. l. soc. Belg. d. chir.*, 1908, viii, 106) reports one case in which M. Verhoogen excluded the bladder from the urinary tract, and a second case in which he did a total extirpation of the bladder with a tumor growing in it. In both cases the ureters were transplanted into the cecum and the latter isolated from the rest of the gastro-intestinal tract, a fistulous tract being made from it to the surface of the abdominal wall. The first was done in a woman, aged sixty-eight years, for invasion of the bladder by a carcinoma of the uterus. After opening the abdomen the right ureter was divided between a ligature below and a forceps above. The upper cut end was introduced and sutured into an opening in the posterior side of the cecum. The same procedure was carried out with respect to the left ureter, which was carried under the peritoneum to the cecum. A rubber drainage tube was introduced to the seat of the anastomoses, to provide against possible leakage. The ileum was then divided close to the cecum and its cecal end closed by a double continuous seromuscular suture. Then the cecum was divided and the two ends closed in a similar manner. The open end

of the ileum was then anastomosed into a lateral opening in the lower end of the ascending colon. The appendix, which was fortunately of a larger caliber than the normal, was opened, a rubber catheter introduced through its lumen into the cecum, and the appendix sutured into the abdominal wound. Fearing that later the lumen of the appendix would close, the operator attached the cecum to the abdominal wall, so that it might be opened subsequently if necessary. The abdominal wound was then closed. During the first twenty-four hours there was no trouble except that it was necessary to change the dressings several times, because they were soaked with urine which indicated leakage at the sutures. On the following day there was severe dyspnoea, and there were rales in the chest. Death occurred in the afternoon. The autopsy showed pulmonary oedema and neoplastic foci in the two lungs. The left ureter was closed at the anastomosis, the right was permeable. The pelves of the two kidneys were much dilated, the cystic parenchyma was very anemic and showed lesions of interstitial nephritis. The second patient in whom the bladder with its tumor was extirpated, and in whom only one ureter was anastomosed to the cecum, the other being ligated and therefore occluded because that kidney was atrophied and functionless, lived only three days.

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**Subtemporal Decompressive Operations for the Intracranial Complications Associated with Bursting Fractures of the Skull.**—CUSHING (*Annals of Surgery*, 1908, xlvii, 641) says that in most fractures of the base of the skull the symptoms are brought about by an increase of intracranial pressure, whether immediate from free extravasation due to laceration of cortical vessels, intermediate, often with a "free interval" of consciousness, when an extravasation outside the dura slowly augments in size, or late, often a matter of a few days when cerebral oedema occurs. During the last three years Cushing has followed the routine of making a subtemporal exploration through a split-muscle incision combined with a subtemporal decompression, namely the removal of a circle of thin bone, about 4.5 cm. in diameter, from under the muscle. A dural opening is also made. The former mortality was about 50 per cent. Of the last 15 cases only 2 have been lost, each from an overlooked extensive intracranial extravasation on the opposite side of the head. The advantages of this method of treatment are as follows: (1) The approach is made through the thinnest part of the skull. (2) The opening is made under the temporal muscle the fibers of which are split and not divided, so that when closed they serve to prevent too great bulging, and serve later to prevent a subsequent obtrusive depression when the normal conditions have been restored. (3) In case there has been a rupture of the meningeal or one of its branches the extradural clot is certainly brought into view by this opening, and as the meningeal vessel is exposed it can be ligated. (4) In all bursting fractures accompanied by laceration of the brain it is the tips of the temporal and base of the frontal lobes which most frequently suffer, and a subdural extravasation from this source can most readily be dealt with through an opening in this situation. (5) In a large proportion of bursting fractures the lines of fracture seek out the midcranial fossa, and hence free bleeding from the base can be

most easily drained through the temporal fossa by drains placed under the temporal lobes. (6) The subsequent œdema and swelling of the brain, which is an almost invariable sequel of any serious cerebral contusion and which is responsible in many cases for the pressure symptoms during the first two weeks, can be best combated by an opening in this situation under the muscle. (7) Aside from the prompt subsidence of the acute symptoms which are often seen after these operations, they appear to lessen many of the unpleasant late sequels, traumatic neuroses, which are so often a feature of the cases which have recovered without operation.

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**Fracture through the Anatomical Neck of the Humerus with Dislocation of the Head.**—BUCHANAN (*Annals of Surgery*, 1908, xlvii, 659) says that fractures through the anatomical neck of the humerus associated with dislocation of the head, present features so distinctive in their mechanism of production, in their pathology, in their amenability to external treatment, and in the nature of their operative treatment, as to place them in a class by themselves. A case of this kind came into Buchanan's hands after ineffectual efforts at reduction had been made. The ordinary signs of dislocation were not present. The rotundity of the shoulder was almost completely preserved. The elbow could be applied to the chest wall and the hand placed on the opposite shoulder. The tuberosities could be felt to rotate under the acromion with the shaft of the humerus. The persistent pain and helplessness of the limb, however, indicated a serious injury and rendered an *x*-ray examination advisable. This showed a fracture of the anatomical neck with subglenoid or axillary dislocation of the head. The head was removed with difficulty by an incision made along the lower border of the anterior axillary fold the fragment being held firmly under the axillary vessels and nerves. Examination of the patient six months after the injury showed the arm to be of normal appearance with very little wasting. Unaided abduction of the arm was possible only to the extent of about 45 degrees. By passive movements the arm could be brought, easily, almost to the horizontal. All movements of the forearm and swinging movements of the limb were satisfactory. Use of the arm was much impaired in last three months, no doubt due to neuritis of the median nerve from pressure of the head prior to its removal. Reduction of the head fragments by external manipulation has been reported, but not verified by the *x*-ray or autopsy. Reduction by open incision has been done in but three cases, with one good result, one fair result, and one result which could be counted fair at the end of seven weeks, the time of the report. Excision of the dislocated head is the operation of choice, having been performed in 14 cases, with 2 results called excellent, 6 good, 1 moderately good, and 2 deaths to its credit.

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**Osteoplastic Resection of the Skull.**—WOOD (*Annals of Surgery*, 1908, xlvii, 645) has so modified the Stellwagen trephine as largely to overcome the objections to its use and to make of it a very useful instrument. The various parts of the modified instrument, which is well illustrated, are as follows: (1) A T-handle, armed with a bone drill. (2) A shaft, to which the handle is adjusted, provided with a fenestrum to accommodate



the radial arm, and a blunt centre-pin at the end. The handle is held to the shaft by a spring, but is instantly released by slight traction. (3) A radial arm which is received in the fenestrum in the shaft, and is secured by a thumb screw. The knife and saw are carried at the outer end of this arm, and are held by a set screw. (4) A radial arm handle, to be adjusted to the extremity of the arm, and used to give the circular motion to the knife and saw. The arm is graduated in inches and centimeters so that it may be instantly adjusted to cut an opening of the desired size. (5) Knife and saws. Wood makes the following claims for the instrument: (1) It enables one to cut an osteoplastic flap of the skull quickly and safely. (2) No injury can possibly be done. The careless or clumsy use of the instrument can do no harm. (3) Every part may be sterilized by boiling. (4) It is always ready for use as there are no complicated parts to get out of order. (5) It is complete in itself and does not depend on electric currents, motors, assistants, or anything but the hands of the operator.

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**The Treatment of Dislocation of the Shoulder-joint Complicated by Fracture of the Upper Extremity of the Humerus.**—MASON (*Annals of Surgery*, 1908, xlvii, 672) says that every dislocation of the shoulder associated with fracture of the upper extremity of the humerus is a grave injury, and is likely to result in serious impairment of function if not promptly treated. Every such injury should be subjected to x-ray examination for accuracy in diagnosis. Gentleness should characterize all manipulative efforts at reduction, and these should never be carried to the point of bruising or lacerating the tissues. Excision should only be practised when reduction by open arthrotomy has failed, or when there is extensive comminution of the upper end of the humerus, or when in fracture of the anatomical neck, the condition of the upper fragment does not justify a reasonable expectation of uniting. After reduction the broken greater tuberosity should be nailed into position if the case is recent, and should be removed if it causes impairment of function in an old case. Failing to reduce by manipulation, immediate arthrotomy with reduction of the dislocation, followed by appropriate treatment for the fracture, has given the best results, and is the ideal method of treatment. Rigid asepsis is essential in securing good results, and these operations should not be undertaken when this cannot be carried out.

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**Some Remarks on the Testicular Manifestations of Gonorrhœal Origin.**—DIND and METRAUX (*Annal. d. mal. d. org. genito-urin.*, 1908, i, 346) say that if the epididymis is the result of infection transmitted by the blood, there should be preceding general symptoms indicating the presence of the infection in the blood. But those are generally absent until the epididymis is developed. As the operative treatment increases it will probably show a greater number of cases in which the gonococcus can be demonstrated. Andry accounted for suppuration in epididymitis by assuming that extension occurred by way of the lymphatics of the spermatic cord and epididymis. Sprecker, Hartung, and Witte have found the gonococcus in abscesses of the epididymis. Baermann found that the abscess was the result of the same organisms

as those producing the urethritis, the gonococcus or others. Schindler recommended in grave febrile cases, with pronounced local infiltration, that the organ be punctured, and suggested that the punctures may be multiple. This treatment gives much relief, lowers the temperature, and decreases the infiltration. This is due to relief of the congestion from the subcutaneous hemorrhages which result. Dind and Metraux did not obtain good results from this method of treatment. They prefer an incision into the inflamed organ, which should be on the dorsal surface of the epididymis, 2 to 3 cm. long, going through the skin, fascia, and superficial layers of the epididymis. This permits an inspection of the tissues, when one may find either a diffused inflammation or intense congestion. The incision gives much hemorrhage and generally exposes some evidence of pus. One may find that the inflammation has become localized, and that one or more purulent foci are distributed throughout the organ, with fungous or necrosed walls. After rubbing away the purulent material with gauze or a blunt curette and arresting the hemorrhage the wound may be sutured, leaving in a gauze drain for twenty-four hours. The operation can be done under cocaine and gives excellent results.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**Diet in Gout.**—SIKES (*Practitioner*, 1908, lxxx, 396) states that there seems to be a general tendency toward the recommendation of a simple mixed diet for the average patient. Also, it is now customary to modify the diet more to suit the individual digestion than to prescribe one that is free from this or that chemical element, as, for example, the quantity of purin. In average patients meat need not be forbidden, but the amount should be restricted to one meat meal in the day. We are coming more to consider the carbohydrate element of the food, and its effect on the liver, as of more importance than was formerly the case. Hence it is advisable to reduce the amount of carbohydrate which is taken in the comparatively pure form, such as potatoes, rice, etc. If we wish the digestion to proceed as normally as possible, and to avoid the absorption of imperfectly elaborated products, it is only rational to prevent the undue dilution of the gastric juice, conse-

quently liquids during meals should be restricted as much as possible. Simple meals, limitation of carbohydrates, restriction of alcohol, and the drinking of non-alcoholic liquids between meals are the important points.

**The Therapeutic Value of Oxygen Inhalations.**—BUREAU (*Gaz. méd. de Nantes*, 1908, xxvi, 161) considers that oxygen inhalation is a most effectual means of combating asphyxia. In certain patients, particularly in bronchopneumonia of infectious nature, influenzal or otherwise, with marked cyanosis, the action of this therapeutic measure is most beneficial. The inhalations are also of some service in the asphyxia of tuberculosis. In other asphyxias their action is dubious. The oxygen should be administered in large amount, the quantity to be regulated by the condition of the patient. The gas should be inhaled until the cyanosis has disappeared, and the patient should be kept under the surveillance of an observer sufficiently experienced to recognize the indications for the renewal of the inhalations, that is, upon the first evidence of a renewal of the cyanosis.

**The Roentgen Rays in Cutaneous Epithelioma.**—DUBREUILH (*Jour. de méd. de Bordeaux*, 1908, xxxviii, 133) cites a number of instances of epithelioma which, he states, show the importance of flexibility in therapeutics. It seems certain that the x-rays are able to cure cutaneous epitheliomas, but it is just as assured that this agent cannot cure this affection in every instance; between these two extremes there are patients to whom the rays are capable of conferring considerable benefit, though not complete cure, if the operator knows how to adapt the treatment to the patient in hand.

**Prophylactic Treatment by Bacterial Inoculation.** RITCHIE (*Edinburgh Med. Jour*, 1908, xxiii, 295) considers that this form of prophylactic treatment, in the ordinary sense of anticipating infection, has enormous possibilities. We are, however, faced with the difficulty of not always knowing what organisms we have to combat. This difficulty, in the case of wounds, operative or accidental, is more apparent than real. If we give a dose of 1000 to 10000 mg. each of *Staphylococcus aureus* and *Streptococcus pyogenes*, and also of *Bacillus coli*, if in the region of a mucous tract, we shall probably cover most eventualities, for other infections are usually secondary. Ritchie gives such an inoculation in all operations with, so far, satisfactory results. In accidental wounds, too, we can similarly control, if not wholly prevent, sup-puration.

**The Treatment of Chilblains.**—GARDINER (*Practitioner*, 1908, lxxx, 251) advises (1) constitutional treatment, consisting of iron, cod-liver oil, and tonics when indicated, the nitrites if there is tendency to angioneurotic disturbances, and, in urticarial patients, the administration of calcium chloride in doses of 15 grains three times daily; (2) local treatment. Foot and hand wear should be loose, warm, and non-irritating. Massage is helpful as a prophylactic, and as local applications ichthyol and formalin are of preëminent value. The former may be used in 10 to 20 per cent. strength with lanolin as an ointment. Spread on linen and worn at night, it often dispels a threatened attack. Formalin should not be

used in the pressure of abrasions, but in their absence may be applied as an ointment of from 10 to 50 per cent. strength, depending on the susceptibility of the patient's skin. If its astringent action goes too far and the skin becomes cracked, the formalin should be stopped and vaseline or lanolin applied. Electricity in the form of galvanism, faradism, the  $x$ -rays, and the high frequency current are often useful. In the ulcerating stage an ointment consisting of mercury ammoniate, 5 grains; ichthyol, 10 minims; powdered starch and zinc oxide, each 2 drams; and vaseline,  $\frac{1}{2}$  ounce, is recommended. Patients who resist the various measures mentioned are likely to have lupus erythematosus and not chilblains.

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**The Scope of Therapeutic Inoculation.**—SANBORN (*Boston Med. and Surg. Jour.*, 1908, clviii, 484) emphasizes the necessity, in attempting the treatment of a number of patients in a general hospital by bacterial vaccines, of being familiar with, and having the laboratory equipment needed to make use of, not only procedures for determining opsonic indices, but also the other methods which may be applicable in the study of questions that arise in the immunization of special patients; with methods of treatment which will act as adjuncts to the bacterial vaccines without access to the laboratory when certain information is needed, is unsatisfactory, and may be a source of damage to the patient, though many infections may be treated with clinical symptoms alone as a guide; on the other hand, the extreme of using the opsonic index to guide, without reference to clinical symptoms, is equally unwise and unscientific. For the successful application of immunization methods one must not only be well grounded in the biology of the infecting agents, their methods of attack within the body, the machinery that the body sets in motion to destroy them, and the effectual procedures to assist the body in its struggle, but also should have the broadest clinical training, in order that the relations of the laboratory and the clinic may be close; that the one may supplement the other in the interest of the individual patient.

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**The Mixed Toxins of Coley in Leukemia.**—LARRABEE (*Boston Med. and Surg. Jour.*, 1908, clviii, 183) has used the mixed toxins of streptococcus and *Bacillus prodigiosus* in four instances of leukemia. One of these showed a degree of improvement amounting to symptomatic recovery which has lasted for upward of four months. Another patient showed considerable temporary improvement; a third showed improvement in weight and general condition only. An instance of acute lymphatic type was uninfluenced. Although two are still under treatment, there does not appear to be much hope of permanent cure. With the effects sometimes obtained with the  $x$ -rays, the author is unable to say that the toxins compare favorably. The toxin treatment is decidedly more painful and dangerous, but it has the advantage that it can be used in many patients when radiotherapy is not available. The conclusion is that the results have been encouraging enough to warrant further trial.

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**Retrorectal Injections of Artificial Serum in Incontinence of Urine.**—JABOULAY (*Tribune médicale*, 1908, xli, 202) has been able to influ-

ence favorably instances of this condition by means of injections of normal saline solution in amount up to about 6 ounces. The needle is inserted just anterior to the coccyx, a finger having been placed in the rectum in order to protect this viscus. To obtain the best results of the treatment several injections may be necessary, and when the affection is due to such causes as preputial adhesions, etc., the treatment is not indicated, but in those forms of incontinence of which the causation is not obvious the injections afford distinct relief, although they may not prove absolutely curative.

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**The Thymus Gland Treatment of Cancer.**—GWYER (*Annals of Surgery* 1908, xlvii, 506) believes that all patients suffering from cancer should be operated upon if the condition permits, and that at present there is no remedy which offers so much chance of cure as does the knife. The value of thymus will be found in the treatment of patients after unsatisfactory operation, such patients as those in whom, at the time of operation, we feel that the entire disease has not been eradicated. Inoperable and advanced cases will be benefited, their lives prolonged, and made enduring, and some may be so improved both locally and constitutionally that operation may become feasible. It would seem that either the action of the thymus continues for a fairly long time, or it so alters constitutional conditions that the tendency to growth is stopped.

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**The Action of Radium on the Blood.**—AUBERTIN and DELAMARRE (*Tribune médicale*, 1908, xli, 170) have studied the modifications of the blood produced by the action of radium on white mice. In about an hour leukocytosis appears, which rapidly gives place to leukopenia, which lasts for some time, but ultimately disappears. If repeated applications of the radium are made, the leukopenia continues and the red cells are diminished in proportion. The spleen presents degenerative changes analogous to those produced by the x-rays. The blood changes take place earlier than do those in the spleen, and short exposures may cause no splenic lesion whatever; here the leukopenia is not due to the degeneration of the lymphoid veins. Radium seems to act upon the deep-lying organs (and especially upon the hemopoietic system) in the same way as do the x rays.

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**Colloidal Metals in Therapeutics.**—DE COSTER (*Revue médico-sociale* 1908, xii, 8) draws the following conclusions from an extensive review of this subject: (1) From a physiological standpoint, colloidal metals are very easily absorbed, no matter what their mode of introduction; they are eliminated by the kidneys and are devoid of toxicity. They produce a thermic reaction, probably the result of increased activity in oxidation, especially in reference to the liver. (2) From a bacteriological standpoint, the nature of the metal employed is important; silver appears to be the most active of those studied. The bactericidal power of the metal is strong in proportion to the perfection of the solution of the metal. (3) From a therapeutic standpoint two series of observations have been made: the first on infectious diseases treated by intravenous, subcutaneous, and intramuscular injections. These injections always caused thermic reactions, characterized first by a rise of temperature, later by a very constant fall. The second series of

observations concerned the local action of the metal upon abscesses and localized infections due to pathogenic microorganisms. Colloidal silver showed itself particularly active in infections due to the streptococcus, the staphylococcus, *Bacillus pyocyaneus*, and the pneumococcus.

**The Treatment of Ophthalmia Neonatorum.**—MAYOU (*Practitioner*, 1908, lxxx, 354) advises the following treatment: In infections of any severity a 2 per cent. solution of silver nitrate should be painted once daily over the lids and fornices. In mild instances, 10 per cent. protargol may be substituted, but the silver salt is much to be preferred. In the intervals of its application the conjunctival sacs should be washed out every hour with 1 to 8000 mercury bichloride. This should be used cold, or even iced, since the cold inhibits the growth of the gonococcus, and at the same time prevents excessive swelling of the lids. The silver nitrate should be rubbed into the conjunctiva of the tarsus and fornix, so that the drug may reach the bottom of the papillæ, but care should be taken not to damage the corneal epithelium. The excess of silver should be neutralized with salt solution. The nurse should be careful against infecting herself. If only one eye is affected, the sound eye should be covered by a shield, or, better, in infants, by cyanide gauze sealed on the nasal side by collodion, or strapping. It should be inspected for the first few days to see if infection has taken place. The treatment should be continued, at least with the lotion, for a month after all discharge has ceased. Mayou has employed antigonococcic serum (horse) in the early stages in four patients, with the idea of trying to shorten the disease, but without definite result.

**Viscum Album in the Arterial Hypertension and Albuminuria of Pregnancy.**—OLIVEAU (*Quinzaine thérapeutique*, 1908, ix, 53) advises the administration of viscum album (mistletoe) in connection with milk diet in this condition. The latter is insufficient to control the symptoms in many instances, and the result is better if the mistletoe, which acts as a reducer of arterial tension, is also prescribed. An aqueous extract of the drug is made by adding to 2½ drams of the dried leaves of viscum album 6½ ounces of boiling distilled water, 5½ grams of sodium chloride; 15 minims of this preparation is injected every twenty-four hours, and, with a milk diet, this form of treatment is said to be quite effective.

## PEDIATRICS.

UNDER THE CHARGE OF

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**A Case of Hirschsprung's Disease, Healed by Entero-anastomosis.**—GERMER (*Deut. Zeit. f. Chir.*, 1907, lxxxix, 385) reports the case of a boy, aged four and a half years, who had difficulty in defecation ever

since his birth; for days he had no bowel movement, and when he had a stool, it was scant and liquid. During the last six months the abdomen had gradually enlarged, until at the time of observation it measured 67 cm. and was of board-like tension. The abdominal and thoracic organs were pushed upward and the abdomen occasionally presented visible peristaltic waves, which demonstrate a markedly dilated colon. The finger introduced into the rectum entered a tremendously dilated gut, the walls of which could not be felt. A rectal tube was inserted, and during the next few weeks the bowel was irrigated twice daily and abdominal massage was practised; much fecal matter was removed, and at the end of the first week the abdomen measured but 57 cm. and the patient seemed considerably better. The visible peristalsis continued, however, and as the abdomen diminished in size a doughy tumor could be made out in the right iliac fossa, which was believed to be fecal material, which the weak intestinal muscle could not move. As symptoms of intoxication developed partly due to a preëxisting bronchitis, an operation was resorted to. The large intestine was found tremendously dilated up to the ileocecal valve, and an anastomosis was therefore performed between the ileum and the lower part of the sigmoid. The patient recovered completely; five weeks after the operation he had voluntary stools and his abdomen measured but 47 cm. Germer calls attention to the importance of cleansing the bowel as much as possible before the operation, to the value of abdominal massage before and after the operation, and to the necessity of using perfectly healthy loops of intestine for the anastomosis.

**The Symptomatology and Etiology of Barlow's Disease.**—ESSER (*Munch. med. Woch.*, 1908, iv, 896) reports a number of cases of Barlow's disease occurring in children who were kept for some time on milk furnished by the city of Bonn. There were 9 girls and 4 boys, varying in age from seven to fourteen months. The symptoms consisted of diminution of appetite, pallor, pain upon being lifted or touched, swelling and deformity of the thighs, bleeding from the gums, ecchymoses, hemorrhage into the cellular tissues about eyes, and hematuria. The blood picture showed an excessive hemoglobinemia, some oligocythemia, poikilocytes, macrocytes, microcytes, normoblasts, polychromatophilia, and basophilic granules within the red corpuscles. The latter were noted especially during the stage of improvement in all the cases. In no instance was a disturbance of leukocytes reported. The milk given the children was sterilized for ten minutes at 102° C., the steam passing through under a pressure of 1½ atmospheres; the process now simply consists of steam at from 98° to 100° passing through for three minutes. The cause of the disease Barlow finds is too long sterilization, as it produces certain toxic substances at the expense of some of the food molecules. All of the patients recovered as soon as antiscorbutic treatment was ordered and the sterilized milk replaced by raw milk. Recovery resulted promptly in the case of a child, in which the hemoglobin had fallen to 20 per cent.

**Intussusception and its Cause.**—W. L. WALLACE (*Jour. Amer. Med. Assoc.*, 1908, 1, 1177) reports the case of a boy of three who had a hydrocephalic head and a crooked spine. He had complained of

abdominal pain for a week, and had vomited repeatedly during the preceding twenty-four hours, the material vomited being a thin bloody substance. He was shocked, markedly thirsty, and absolutely constipated. A diagnosis of high intussusception was made; the operation revealed a small enteric intussusception at the ileocecal valve, and a complete sausage shaped intussusception in the jejunum. Five weeks later complete obstruction occurred again, and adhesions were found tying the bowels to the mesentery at the jejunal site; the same condition recurred eight months later and six weeks thereafter obstruction occurred again. Immediate operation revealed a blocking of the bloodvessels of the mesentery and a marked distention of the corresponding segment of the bowel; the intestine above this was pushing into it as if trying to reinforce the weak segment by the invagination. Wallace refers to the two theories of the cause of intussusception: spasm and paralysis. His case supports the latter theory; the spasm precedes the invagination, tiring the bowel out so that paralysis is the result and this then is followed by the invagination. The paralysis also interferes with the peritoneal blood supply, and this sets up enough peritonitis to produce adhesions and prevent spontaneous reduction.

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**Pemphigus Neonatorum Simplex Congenitus.**—A. LABGARDT and J. WALLART (*Ztschr. f. Geburtsh., und Gynäk.*, 1908, lxi, 600) have been able to collect 13 cases of non-syphilitic, congenital simple pemphigus from the literature; the first case dates back to 1794. They are able to add 3 of their own to this small list. In 2 of their cases the eruption was general, consisting of vesicles of various sizes surrounded by a red areola; the vesicular contents were serous, seropurulent, and purulent; in the third case there were but two large vesicles over the upper eyelids. In one of the cases staphylococci and streptococci were cultivated from the vesicular contents. In two of the instances the mothers were perfectly well, while in the third there was a small suppurating wound, enlarged glands at the elbow and in the axilla. The vesicles dried up promptly, the children remaining well thereafter. In none of the cases was there the slightest indication of syphilis in either mother or child. The cause of the disturbance in their opinion is in most cases a transference of microorganisms from mother to child; in other instances a sore throat or other slight infection of the mother may give rise to a toxemia, which is of sufficient intensity to induce an exanthem in the foetus.

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**Ophthalmia Neonatorum: An Experiment In Treatment.**—A. N. WALKER (*Lancet*, 1908, i, 1267) recommends the following vigorous treatment in all incipient cases of ophthalmia neonatorum; the method was first employed in the cases of a physician and two nurses who had been attending ophthalmia cases: As soon as it was noted that their eyes were injected and that they were discharging a thin mucopurulent secretion, a 0.5 per cent. solution of zinc chloride was dropped into the eyes at frequent intervals for twenty-four hours, and this was followed the next day with a 25 per cent. solution of argyrol. All three patients recovered within forty-eight hours. In England all births must be reported to the proper authorities within thirty-six hours, and a lady inspector must visit all the cases attended only by midwives or handy



women. If a baby is found with discharging eyes medical aid must be had at once, and if the discharge is diagnosticated as gonorrhoeal, an ambulance furnished by the city conveys mother and baby to an isolation ward in the ophthalmic hospital, where the above-mentioned treatment is carried out. In nearly all instances the result is very satisfactory as compared with the older method; the average time of recovery for patients treated in the hospital, according to the older method, is two months.

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**Pathology and Treatment of Inguinal Hernia in Children.**—C. H. FAGGE (*Lancet*, 1908, i, 1270) reports having operated successfully upon 78 children suffering with inguinal hernia. All cases of hernia, he says, are primarily due to a developmental defect, either partial or complete persistence of the embryonic processus vaginalis. This refers not only to what is usually termed "congenital hernia," but also to hernia said to be induced by marked straining, coughing, phimosis, etc.; the patent funicular process is the chief factor in all cases. The only condition that may cause some difficulty in diagnosis is congenital hydrocele. The latter is irreducible with the child in the upright posture, the fluid returning to the abdominal cavity spontaneously when the child lies down and returning slowly to the scrotum when the upright position is again resumed. Circumcision neither prevents nor cures a hernia; a truss must be applied as soon as the hernia appears; it must be worn every day and in some cases even at night, and it is only after several years that in a few cases a cure will be obtained. Indications for operation are: (1) Herniæ which cannot be kept up by trusses, or which are painful when a truss is worn; (2) large scrotal herniæ, which have stretched the inguinal canal considerably and therefore render trusses necessary throughout life; (3) the association of an undescended testicle with a hernia; and (4) a hernia which has been irreducible on a previous occasion. Taxis should never be attempted. Strangulation is an immediate indication. The operation may be performed during the first months of life and is usually well borne then. Sometimes early operation has advantages: secondary changes in the neck of the sac and in the posterior wall of the inguinal canal have not taken place yet. He described the technique and results in detail.

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## OBSTETRICS.

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UNDER THE CHARGE OF

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**High Rectocele after Perineal Repair.**—DICKINSON (*Amer. Jour. Obstet.*, March, 1908) draws attention to this condition, and believes that it can best be prevented by digital rectal examination of the septum before anesthesia, to determine the condition of the tissues before they

are relaxed with ether. The operator can then decide how high up the weak spot in the rectovaginal septum extends and where the edges of the muscle are. To determine how large a surface should be denuded, artery forceps are attached to the lowest recognizable end of the hymen on both sides. These are brought together over the tips of two fingers until a snug fit is obtained. The forceps are then left in place, but dropped. The second pair are attached to the lateral walls of the vagina, and make the same test, while the fifth clamp catches the farthest spot of the rectocele. With the clamps in position, the knife outlines the area to be denuded, and the clamps may then be removed before suture. To determine the edges of the fascia and muscle, a ball of gauze is inserted into the rectum and pressed forward to carry the rectal wall forward. The upper edge of the sphincter is easily found and the stitches are placed. Before tying the stitches they should be drawn up so that the raw surface is closed. The ball of gauze in the rectum is then brought down against the newly closed tissue. If it cannot pass, it is inferred that the closure will be successful. Women over fifty or sixty years, whose tissues are prematurely relaxed, should take especial precautions after operation. When the pelvic floor has become atrophied especial precautions are also necessary, as in the case of those patients in whom the rectum is habitually distended, or in whom there is especial resistance at the anal opening. Such patients should have their convalescence prolonged for three or four weeks, enemas of oil should be given at evening to be retained until the morning to secure a soft movement, and the patients should avoid corset pressure or heavy skirts. Care should also be taken to guard against irritability of the sphincter muscle of the bowel.

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**The Importance of Rest in the Puerperal Period.**—MARTIN (*Monatssch. f. Geb. und Gyn.*, 1908, xxvii, Heft 2) studied 100 cases in the puerperal period, with the idea of determining the influence of rest or motion after labor. By getting up, Martin understands that the patient sits quietly in a practically upright position, with a firm bandage around the abdomen. Such patients are not allowed to move about freely, nor to do any special work with the hands and arms. These patients leave their beds from fifteen to twenty-four hours after the completion of labor. In the next seven days they are allowed to be out of bed two hours in the forenoon and two hours in the afternoon. If the pulse or temperature rises, or any disturbance occurs, they are forbidden to sit up. When gonorrhœa has been present, patients are not allowed to sit up so early, but must remain recumbent until the pulse and temperature have become normal. Among these patients there were 62 primiparæ and 38 multiparæ. Infection developed on the third day in 4, on the fourth day in 2, on the fifth day in 5, and on the seventh day in 1. In the last case the contents of the uterus showed the presence of gonococci, and in the other cases, streptococci, staphylococci, or diplococci were present. In some of these cases the pulse on the sixth or seventh day was comparatively higher than the temperature. In but one patient did the temperature rise above 102.5° F.; and in none of the cases did fever last longer than two days. The morbidity of the series was 13 per cent. Involution proceeded well and in no case was it necessary

to use ergot to hasten the process. On the seventh day the uterus was anteflexed and the size of a small fist. The advantage in this treatment is seen in the improved emptying of the intestine and bladder, as patients were spared the use of cathartic medicines and the catheter. No influence upon the ability of the mother to nurse her child could be detected. The younger women improved very rapidly, none of them was faint, and all looked much better for the change in posture. In none of these cases was there an abnormal position or dislocation of the uterus, nor could there be observed any tendency to prolapse of the vagina or uterus. It is sometimes alleged that the early assumption of the upright posture is followed by an increased danger of embolism. The statistics of large numbers of hospital patients who have gotten up early do not show that such has been the case. The precaution is taken to watch the pulse, and should this become rapid the patient is obliged to lie down. As regards the development of infection in 1000 cases treated by the usual method of prolonged rest, the morbidity from infection was 18.5 per cent. In the present series of cases the entire morbidity was 13 per cent. It is obvious that if a patient were infected, and moved about soon after labor, such motion must tend to spread infective bacteria throughout the tissues. Puerperal patients should not get up early unless preëxisting infection can be positively excluded, and the patients are under medical control.

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**Labor Obstructed by an Ovarian Dermoid Retained for Two Years in the Pelvis.**—DORAN (*Jour. of Obstet. and Gyn. Brit. Empire*, February, 1908) reports the case of a patient who was found to have a pelvic tumor during her third stage of labor. The attending physician succeeded in pushing the tumor out of the pelvis, and the child was born living. Six weeks after confinement, the patient had sharp pain in the right iliac region, suggestive of appendicitis. This pain subsided, but the patient was found to have in the pelvic cavity a firm elastic mass which had displaced the uterus forward. She declined operation. About eighteen months afterward the patient returned for operation, stating that she had frequent attacks of abdominal pain which was very acute. The pelvic tumor was found to be a dermoid of the right ovary, weighing one pound, five ounces. It was twisted with two turns of the pedicle from left to right, and was livid through the engorgement of its veins. The tumor had fallen back behind the uterus and left ovary, which were pushed upward and forward. When the pedicle was untwisted the lividity disappeared, but the tissues of the pedicle were free from atrophic changes. There were no adhesions, and the appendix was normal. The tumor was readily removed. It contained about one pound of grease with hair of a light auburn color. The tumor had remained in the pelvis for two years without contracting adhesions, and, although it fitted closely into the pelvic cavity it had undergone rotation upon its axis. The torsion was partially reduced at the end of each attack. As the pedicle was upon the right side, the pain naturally suggested disease of the appendix.

## GYNECOLOGY.

UNDER THE CHARGE OF

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**Adenomyoma of the Uterus.**—T. S. CULLEN (*Jour. Amer. Med. Assoc.*, 1908, 1, 107) reports 22 cases of adenomyoma that he had examined previously, and states that he has been surprised by the frequency of these growths, 5 per cent. of all myomas proving to be of this character. He pays tribute to von Recklinghausen for his masterly work on this subject, published in 1896. These growths, containing gland elements and myomatous tissue, form a distinct type of neoplasm that is easily recognized microscopically. The mucosa is usually smooth and has an intact epithelium. The glands appear normal, but the stroma of the mucosa is often oedematous or rarefied. The diffuse thickening in the uterine wall consists of the characteristic myomatous tissue, but the muscle bundles are much more interlaced than in ordinary myomas. Along the border of the growth the myomatous cells gradually blend into the muscle cells. Usually the mucosa is not encroached upon, but, on the contrary, is seen to have prolongations or even isolated portions ("islands") in the myomatous tissue, with the stroma always visible between the epithelium and the myomatous tissue. Although associated with carcinoma of the cervix and body of the ureters in 5 of the 73 specimens he has examined, Cullen agrees with von Recklinghausen and Welch in concluding they are benign tumors, for which Welch proposed the name "adenomyoma diffusum benignum."

**Myomectomy or Hysterectomy.**—JAMES N. WEST (*Amer. Jour. Obst.*, 1907, lvi, 700) states that he has performed myomectomy on 31 patients, 2 of whom died, and that during the past three years he has done 40 consecutive, successful hysterectomies for fibroids of the uterus. Pregnancy followed myomectomy in 4 cases. West opposes the principle of removing all fibroids, and gives the following reasons for surgical treatment of them: (1) Great size, causing visceral changes, exhaustion, and inconvenience; (2) rapid growth or pain and hemorrhages, indicating that the tumor may be malignant; (3) pressure upon ureter, bladder, rectum, or intestine, interfering with the function of these structure; (4) hemorrhage, which cannot be controlled except by radical operation; (5) interference with labor, as in a tumor so situated in the pregnant uterus as to make normal labor impossible; (6) causing sterility, as when a tumor causes frequent abortions or prevents fecundation; (7) pedunculated tumors, or indications of necrosis; (8) various complications may exist in coincidence with the tumor which, taken together with it, will prove sufficient indication for operation. He urges myomectomy in a liberal portion of the operative cases.

**The Relations Between the Ovaries and the Uterus.**—F. DAEL (*Surg., Gyn., and Obst.*, 1908, vi, 153) believes his experiments on guinea-pigs and white rats disprove Fraenkel's conclusions that menstruation is caused by the secretory action of the corpus luteum; that it is not the pressure of the growing follicle upon the ovarian nerves, but the action of the corpus luteum, that causes menstruation, and that that structure causes every four weeks the cyclical hyperemia of the uterus which leads either to pregnancy or to menstruation. Dael states that: (1) The assumption that, after rupture of the follicle, the development of the corpus luteum produces menstruation compels one to assume, furthermore, that the maturation and rupture of the follicle and menstruation are in a regular causal relation to each other, which would contradict the extensive observations of Leopold and Mironoff; (2) as in animals rut continues for weeks, whereas, in the human, menstruation is concluded in from two to five days, we must logically, on the basis of Fraenkel's hypothesis, see the cause of this phenomenon in the fact that in animals several follicles undergo maturation and burst, consequently forming several corpus lutea in succession, thus making the specific action (not only of the vasomotor reflexes) continuous. Dael believes he is justified in the conclusion that even if the theory of Fraenkel is confined to the statement that the origin of menstruation and of rut is to be ascribed to the specific action of the internal secretion of the corpus luteum, this function of the corpus luteum is, at the present stage of researches, to be regarded as an hypothesis only. His experiments led Dael to state that bilateral ovariectomy in the pregnant animal always interrupts pregnancy during more than the first half of its duration. It is well known that this deduction does not apply to the human subject, as in women pregnancy at various stages has thus been tested and found quite able to resist such influence.

**Temporary Ureterovaginal Fistula after Panhysterectomy for Fibroid of the Uterus.**—ERNEST JONAS (*Amer. Jour. Obst.*, 1907, lvi, 132) reports a case of this kind that healed spontaneously. It developed a few days after operation, and was easily differentiated by following the recommendation of Völker and Joseph to inject into the gluteal region 4 c.c. of a 4 per cent. solution of indigo carmine and twenty minutes later inspect the mouths of the ureters, which demonstrated that no urine was entering the bladder from the affected side. In this examination Jonas noticed a ureteral contraction similar to that when urine is discharged from the ureter, but none was being forced out. Jonas regards this as a very important differential point between complete and partial severing of a ureter. Jonas prefers complete to partial hysterectomy for uterine fibroids, and makes a plea for delay in operation for such fistula.

**The Influence of the Central Nervous System in the Causation of Uterine Hemorrhage.**—H. EHRENFEST (*Gyn. Trans.*, 1907, xxxii, 522) believes many cases of uterine hemorrhage are not due to pathological conditions of the uterus or other pelvic organs, but to impulses from the central nervous system. But such influences Ehrenfest holds must be limited to the following physiological and histological facts: (1) The blood circulation in the uterus in a very marked degree stands under

the influence of the vasomotor system, the uterus being an erectile organ. (2) The uterine musculature shows rhythmic spontaneous contractions. (3) Changes in the tonus of both the uterine musculature and vessel walls are subject to the influence of the central nervous system. (4) Uterine contractions at times (as when the impulse reaches the uterus by way of the *nervi erigentes*) is accompanied by active vasodilation. (5) The sudden cessation of a menstrual flow or a temporary amenorrhoea developing as the result of an emotion, or in the course of certain diseases of the nervous system, often cannot be due to organic lesions in the uterus or ovaries. (6) The sudden appearance of hemorrhage as the result of a mental shock can not be explained, like the menstrual flow, as immediately due to certain degenerative processes in the walls of the endometrial vessels. (7) A sclerosis of some of the arterial vessels must be considered a physiological condition in a multiparous uterus.

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**Scopolamine-Morphine Anesthesia in Gynecology.**—EMIL RIES (*Amer. Jour. Obst.*, 1908, lvii, 204), after operating 414 times, about half of which were abdominal sections, makes the following statements: From the time of the first injection to the beginning of the operation the patient should be kept very quiet in a dark room to induce sleep. During the operation the patient may appear to be sleeping and yet be quite able to hear conversation. If aroused during operation, all surgical procedures should be suspended until the patient is again quite. In about three-fourths of his cases ether or chloroform inhalation was necessary. The vomiting in such cases was 60 per cent. when chloroform was used, and but 36 per cent. when ether was employed.

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**The Degenerating, Complicating, and Associate Conditions in 3561 Cases of Fibromyoma of the Uterus.**—STEPHEN E. TRACY (*Surg., Gyn., and Obst.*, 1908, vi, 246) has carefully studied the statistics of 3561 cases of fibromyoma of the uterus reported by others and finds complications recorded 1147 times. Of the 114 cases of degenerations noted 74 (64.9 per cent.) occurred after the age of forty years. Cancer was found in the body of the uterus 63 times, and in the cervix 25 times. Chorio-epithelioma was present in 2 and sarcoma in 54 of them. Thus malignant degeneration of the uterus existed in 144 (4 per cent.) of the cases. Tracy concludes: (1) A large percentage of fibromyomas of the uterus undergo some form of degeneration, but the majority (64.9 per cent.) of degenerations take place in women who are forty or more years of age; in other words, after the menopause. (2) Fibromyomas of the uterus and visceral degenerations are found associated in a large number of cases. (3) Young women who are anxious for maternity and possess small tumors which are causing no symptoms, need not be subjected to operation, but should be instructed to report for examination as soon as symptoms develop. (4) All fibromyomas of the uterus which produce symptoms, regardless of the age of the patient, and all fibromyomas in women forty or more years of age, should be removed when diagnosed, because the mortality following operation, below 5 per cent., is less than the risk of carrying the tumor, as from 12 to 14 per cent. of these patients would die if not subjected to operation. (5)

Supravaginal hysterectomy is the operation of election because of the ease and rapidity of its execution, and because it is followed by the lowest mortality; it should be performed in all cases in which a myomectomy is not indicated and in which panhysterectomy is not demanded. (6) Many of the associate conditions would cause death if the patients were not subjected to operation, but the mortality in these cases should not be added to the estimated mortality of fibromyomas, as they are independent lesions and in no way connected with the tumor except that the conditions co-exist. (7) A thorough pathological study should be made of all fibromyomas of the uterus which are removed, because of the malignant changes and the degenerations which take place in these tumors.

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**Intestinal Occlusion Following Extirpation of Uterine Fibroids of Large Volume.**—J. BOECKEL (*Ann. de gyn. et d'obst.*, 1908, v, 154) reports a case of this character in which he removed an old uterine fibroid mass weighing more than twenty-four pounds by total abdominal panhysterectomy, and in which ten days later for intestinal occlusion he was obliged to re-open the abdomen and relieve an angulation of the transverse colon and do a colopecty. The angulation was in the pelvis and the arms of the V-shaped transverse colon were directed toward the splenic flexure and the cecum.

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**Regression and Calcareous Degeneration of Carcinoma.**—B. H. WELLS (*Amer. Jour. Obst.*, 1908, lvii, 403) reports a case that he saw first in December, 1898, in a married nullipara aged thirty-three years. She had noticed for a year a painful tumor of the uterus. Wells found the uterus was immovable with the fundus extending about two inches above the pubes and rough, irregular, and nodular in outline, and bleeding followed the examination. Upon abdominal section the nodules thought to be cancer were found to extend into the broad ligament and to adherent coils of intestine and omentum. Nothing was removed except a small nodule which microscopically was found to be adeno-carcinoma. June 25, 1903, Wells saw the patient again. She stated that after operation she had improved for several months and then failed materially. At this time the disease was found proliferating in the vagina. From November, 1903, to the date of her death, March 22, 1905, she suffered from hemorrhages, but at the latter date the masses in the abdomen had practically disappeared. At the autopsy the peritoneum covering the intestinal and parietal wall was studded with small, round, hard, white particles varying in size from that of a mustard seed to that of a bean. The mesentery was a dense, fibrous mass several inches in thickness and was covered with masses of little particles. The pelvis was empty with no evidence of the uterus, tubes, or ovaries. There was no mass in the vagina, and its mucosa was everywhere smooth. The small particles removed were examined by Dr. Jeffries, pathologist to the New York Polyclinic, and after decalcification by him sections were made which showed glandular carcinoma infiltrated with many calcareous pearls.

## DERMATOLOGY.

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 UNDER THE CHARGE OF

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**Epitheliomatosis of Solar Origin.**—DUBREUILH (*Annales de dermat. et de syphilographie*, 1907, No 6), who has been studying the statistics of the Dermatological Clinic of Bordeaux with the view of ascertaining the effect of exposure to sunlight upon the occurrence of epithelioma, finds that senile keratoma, which is the first stage of epitheliomatosis, is observed with greatest frequency in those who live in the open air, and that in these it is only the exposed parts which are affected. Its regional distribution is determined not by anatomical conditions, but by the disposition of the clothing. The ears, frequently attacked in men, are entirely free in women who wear a handkerchief, or are affected only in those parts not covered by the handkerchief. Keratosis is not a purely senile alteration, since it may exist in children with xeroderma pigmentosum. Its occurrence is facilitated by age, which is the most important among the predisposing causes, but it is determined by the action of light. While insolation is the efficient determining cause of keratosis and epitheliomatosis, certain predisposing causes such as heredity and the structure of the skin, are not without influence. Dubreuilh concludes that senile epitheliomatosis of the face is not solely the result of old age; it is, above all the, result of chronic insolation and ought to be considered as closely related to chronic radiodermatitis. It affects particularly farmers and all those who work in the full sunlight. Blondes, whose skin contains but little pigment, seem to be more frequently attacked than brunettes, and much more frequently than individuals of the colored race. It is a disease essentially rural.

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**Cancer of the Mammary Gland Presenting the Clinical Picture of Paget's Disease.**—KYRLE (*Archiv f. dermat. und syph.*, Band lxxxiii, Heft 2) reports a case of adenocarcinoma of the mammary gland which presented a typical picture of Paget's disease. The patient was a married woman, thirty-nine years old, who presented on the left breast, in the region of the nipple, a brownish-red, sharply circumscribed patch, about 6 cm. in diameter, covered with thin, yellowish scales. The surrounding non-ulcerated skin showed several radiating rhagades, while in the middle of the patch was a triangular, flat, circumscribed erosion, oozing in places, but covered for the most part by yellow crusts. The disease had lasted about eighteen months, and was believed by the patient to be due to an injury received from running against the corner of a table. In addition to the external disease palpation revealed a walnut-sized lobed tumor in the depths of the mammary gland. Micro-



scopic study of the diseased areola and of the breast-tumor showed that, without doubt, the latter was the primary affection which, spreading in a retrograde direction through the nipple, gave rise to a secondary cancerous affection of the areola. The author believes that there is no uniform anatomicopathological substratum for Paget's disease, since at one time a squamous-celled, at another a cylindrical-celled or gland cancer may produce the picture of this disease, the flat epithelium of the areola, the epithelium lining the milk ducts, or the parenchyma of the milk glands furnishing the matrix for the carcinoma.

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**Epithelioma Adenoides Cysticum.**—CSILLAG (*Archiv f. Derm. und Syph.*, Band lxxx, Heft 2), from a study of two cases observed in a mother and daughter, concludes that the little tumors of epithelioma adenoides cysticum are composed of undifferentiated embryonal epithelial cells, and have their origin partly immediately from the epidermis and partly from the external root sheath of the hair follicle. The cysts which are found in the tumors are of two kinds: (a) small cysts which arise from colloid degeneration of the tumor cells, and (b) large retention cysts resulting from the snaring off of the follicles and sebaceous glands. The milium-like structures seen in the tumors correspond microscopically to the retention cysts of the follicles and sebaceous glands.

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**The Bacillary Etiology of Folliculitis.**—LEINER and SPIELER (*Archiv. f. Derm. und Syph.*, Band lxxxi, Heft 2 u.3), removing lesions with the sharp curette from two cases of folliculitis following measles and scarlatina, respectively, rubbed them up with sterile bouillon and injected the emulsion thus made into sound guinea-pigs, partly subcutaneously and partly into the peritoneal cavity. In animals thus injected tuberculous lesions were found from one week to two months later in several of the viscera and lymphatic glands, tubercle bacilli being demonstrable in such lesions. The authors conclude that these experiments establish the bacillary origin of folliculitis.

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**The Therapy of Lichen Ruber Planus.**—VÖRNER (*Archiv f. Derm. und Syph.*, Band lxxxii, Heft 3) finds protective bandages and ointments as recommended by Seifert in the treatment of lichen ruber planus useful, but does not believe that the benefit following their use arises from the protection of the skin against external injury. In those cases in which localized patches remain after the internal use of arsenic the author has successfully employed this drug externally as a 0.5 per cent. ointment. In cases in which the disease is limited to the legs the use of bandages and arsenical ointment alone may be sufficient to effect a cure. The therapeutic results following the use of bandages upon the legs in lichen of this region are due, according to Vörner, to support of the veins, and not to the protection which they afford against injury.

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**A Fatal Case of Acute Lupus Erythematosus.**—SHORT (*Brit. Jour. Dermat.*, August, 1907) reports a fatal case of erythematous lupus. The patient was a woman, aged twenty-eight years, who had been ill about four months before coming under observation, the first evidence of the disease being noticed upon the tips of the fingers and toes and on the

lobules of the ears. Upon her admission to the hospital there was diffuse swelling of the bridge of the nose and a red patch on the left cheek over the malar region whose surface was rough and dry. The finger tips and some of the toes were red and desquamating. A week later blebs containing pus appeared on a finger and a toe; and two weeks after, the eruption on the left cheek became worse, and a similar patch appeared on the right cheek and in the eyebrows. Follicular ulcers appeared on the roof of the mouth, the feet and vulva became edematous, and the lymphatic glands generally became hard and tender. About five weeks after admission to the hospital the patient had a general convulsion followed by unconsciousness and vomiting; this was followed by a short period of improvement, when vomiting began again, with frequent twitchings and convulsions. The eruption occupied the greater part of the face at this time, which was greatly swollen, but the trunk and limbs remained free except for two small slightly scaly patches at the point of the left elbow. Pneumonia now developed, and the patient died eight weeks after her admission. Microscopic examination of the skin of the face and of the toes showed a well-marked hyperkeratosis of the gland ducts. The fibers of the cutis appeared to be undergoing degenerative changes, as shown by a loss of characteristic staining reaction. Clumps of lymphocytes and fibroblasts were found with numerous plasma cells. Polymorphonuclears were not numerous.

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## PATHOLOGY AND BACTERIOLOGY.

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**The Influence of the Antiferment of the Blood upon the Proteolytic Leukocytic Ferment.**—It has been shown by Müller and Jochmann (and by Opie too, in this country) that when fresh blood serum or blood plasma is added either to leukocytes of the blood or of inflammatory exudates, that these cells lose their power of digesting coagulated proteids, while leukocytes washed free of blood serum possess in a marked degree this proteolytic action when brought in contact with coagulated serum at 37° C. or 50° C. WIEN (*Deut. Arch. f. klin. Med.*, 1907, lixi, 456), by using the method adopted by Jochmann and Müller, has tested the antileukoproteolytic action of the blood serum in 72 cases, which include various acute and chronic diseases. Löffler's blood serum coagulated in Petrie dishes served as the medium. Upon these plates is mixed 1 oese of pus and 1, 2, 3, 4, etc., oese of diluted blood serum. The degree and inhibition of proteolysis was measured by the cupping or lack of cupping of the surface of the blood serum. It was found that

with normal serum 5 ccs diluted 1 to 5 with water was sufficient to inhibit the action of 1 ccs of pus. In many conditions the antiferment action of the serum was not altered, but in cases of acute infections in which there was marked leukocytosis with evidence of destruction of the leukocytes the antiferment action of the serum was decreased. In one case of pneumonia Wien confirms Bittorf's work, and finds the antiferment action greatly reduced at the crisis, and increased to normal or a little above normal immediately after the attack. In uncomplicated tuberculosis the antiferment action of the blood serum was constantly increased. Wien considers that when there is an excessive destruction of leukocytes in the body the antiferment is bound by the degenerating leukocytes, and therefore the amount is decreased in the serum.

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**The Serum Diagnosis of Syphilis.**—Since the original observations of Wassermann upon the diversion of the complement by the mixture of the serum from a syphilitic and an emulsion of organs infected with syphilis, the serum diagnosis of syphilis has assumed a practical value. It was soon found that an alcoholic extract of syphilitic liver acted as well as an emulsion, while later Landsteiner showed that an alcoholic extract of normal liver was quite as efficient as the extract of a syphilitic organ. It was finally discovered that the substance in the liver upon which this reaction was dependent was lecithin. Porges, working along these lines of investigation, pointed out the fact that when lecithin was brought in contact with the serum from a syphilitic patient a precipitate appeared after an interval of twenty hours. This reaction seemed to be specific for the serum of syphilitics. The method which he described was quite simple. Equal volumes of blood serum (0.2 c.c.) and a lecithin suspension in physiological salt solution containing 0.5 per cent. carbolic acid were mixed and allowed to stand for twenty hours. A positive reaction at the end of this time consisted in the formation of a precipitate in the tube. KLAUSNER (*Wien. klin. Woch.*, 1908, xxi, 214), while testing the efficiency of this reaction, discovered that if 0.2 c.c. of the blood serum of a syphilitic was mixed simply with 0.7 c.c. of distilled water, a flocculent precipitate formed at the bottom of the tube after an interval of one to fifteen hours. This precipitate measured from 2 to 4 mm. in height. It was considered to be globulin. With the serum from thirty-one syphilitics the reaction was performed fifty times without a negative result. With 23 control sera the reaction was obtained twice, once in a case of typhoid fever and once in a case of pneumonia.

NOBL (*Wien. klin. Woch.*, 1908, xxi, 287) reports the results of his investigations concerning the accuracy of both the methods of Porges and of Klausner. The reaction of Porges was tried in 83 cases of syphilis. The serum from 68 of these gave a positive result. Of the 68 cases, 36 had manifest symptoms of syphilis, although the duration of the disease varied from a few weeks to many years. In 32 cases there were no evident symptoms of syphilis when the blood serum was tested. Of the 15 patients from whom the serum gave a negative reaction, 8 were in a period of latency, while 7 had recurrent exanthemata or localized gummatous changes. Of the total number of syphilitics, the blood serum gave the precipitation phenomenon in 81.8 per cent.

This percentage of positive results compares very favorably with those obtained by the more elaborate method of complement diversion. By the latter method the highest percentages of positive reactions that have been reported vary between 80 per cent. and 84 per cent. With the Klausner method the precipitate was not obtained with such constancy. It was present in but 21 of 38 cases of known syphilis or in 55 per cent. of the cases. To compare the two methods more accurately, specimens of blood serum from 28 cases of syphilis were mixed at the same time with the lecithin suspension and with distilled water. In every case the method of Porges gave a positive result, whereas in 12 cases the method of Klausner failed. Nobl concludes that this simple method devised by Porges promises to be of great assistance and importance in the diagnosis of syphilis.

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**The Fermentation of Glucosides by Bacteria of the Typhoid-Colon Group and the Acquisition of new Properties of Fermentation by such Bacteria.**—

TWORT (*Cent. f. Bakt. und Parasitenk.*, 1907, xl, 508) has studied the fermentation reactions of 44 strains and varieties of bacteria of the typhoid colon groups upon 49 different glucosides. Of these 49 glucosides, 27 were acted upon by at least one of the bacteria used; but very marked variations were found between fermentative properties of the single members of the subgroups, which, in most instances, were as striking as the variations between the subgroups themselves. Probably the most important part of the work was the demonstration of an artificial variation in the properties of a single strain of bacteria to ferment sugars. By growing, through several generations, one bacterium in a 2 per cent. solution of a sugar, which at first it would not attack, the organism gradually acquired artificially the power of fermenting this sugar. Thus, it was possible to obtain strains of *Bacillus typhous* which fermented dultcit and lactose. By this process it was possible so to alter, in a comparatively short time, the cultural characteristics of certain pathogenic bacteria that they were scarcely recognizable. Such experiments demonstrate the difficulty of recognizing typhoid bacilli which have been recovered from water or sewage, in which perhaps for many generations they have lived under saprophytic conditions. Twort also suggests that if pathogenic bacteria may assume at least some of the characteristics of nearly allied saprophytic strains when cultivated outside the body, non-pathogenic bacteria may lose some of their saprophytic properties when introduced into the body, perhaps the intestinal canal, and assume pathogenic properties.

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THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES.

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ORIGINAL ARTICLES.

**THE RELATIONS OF THE FEMALE REPRODUCTIVE ORGANS TO  
INTERNAL DISEASES.<sup>1</sup>**

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SINCE through the coöperation of surgery with internal medicine a border zone of greatest productiveness has been developed, it is perhaps opportune that the border zone between gynecology and internal medicine should likewise be cultivated more than has heretofore been done. A not inconsiderable amount of pioneer work has already been contributed. In undertaking a sketch of this field, it will be of advantage: (I) To mention those internal diseases which have been observed in connection with the physiological processes of the female generative organs, namely, puberty, pregnancy, and the menopause; (II) to consider the significance of the pathological processes in the female reproductive organs which give rise to medical conditions; and (III) to discuss the relation of certain internal diseases to disorders of the female reproductive apparatus.

I. The period of puberty induces apparently much more marked disturbances in the female than in the male, and, moreover, in the somatic than in the psychic aspect. In regard to the somatic manifestations of disease, we are reminded of chlorosis, a prerogative of the female sex, which appears to be associated with insufficient hemoglobin formation. We do not find, however, sufficient evidence to prove an injury of the red blood disks already

<sup>1</sup> An amplification and revision of an address delivered at a meeting of the Association of German Physicians of New York, April 15, 1907.

formed and of an increased destruction of the hemoglobin therein contained. In any event, the loss of blood during menstruation is insufficient to explain the enormous reduction in the hemoglobin which is found in chlorosis. In relation to the total volume of the blood of the body, the hemoglobin in chlorosis, approximately estimated, is often only 200 grams, while in a healthy girl it amounts to about 600 grams. During a single menstruation, as Hoppe-Seyler has shown, only about 8 grams of hemoglobin is lost.

It is worthy of note that, during puberty, thyroid enlargement has not infrequently been observed; this, as we shall see, may accompany all later phases of the sexual life of woman. This enlargement of the thyroid, which, moreover, is observed with equal frequency during puberty in the male sex, is usually accompanied by palpitation, rapid pulse, irritability, and more easily induced bodily than mental fatigue, and deserves the serious attention of those responsible for bringing up children as well as of physicians. It is, however, doubtful whether all cases of abnormal irritability and rapidity of the heart action which occur during puberty are associated with disorder of the thyroid gland. Frequently, one obtains the impression, in many of these cases, that they are rather the consequence of excessive sexual excitement and particularly masturbation; and often when growth is over-rapid, there are indications of irritability and, indeed, insufficiency of cardiac action, with diminished blood pressure and tendency to syncope.

In contrast to the thyroid heart of puberty, there is sometimes found, associated with evident abnormal smallness of the thyroid, a certain mental sluggishness and the characteristic symptom-complex of juvenile *adipositas nimia*, which, off-hand, must not be regarded as identical with juvenile *myxœdema*.

The psychic changes which develop during puberty are very peculiar. I do not refer to the special psychoses which appear at this time, but to those slight psychic disturbances which are too insignificant to be included within the domain of disease, but which however, can give rise to many difficulties in the training of children. They, for the most part, manifest themselves by an overemphasis of the psychic life, by a tendency to mysticism, or in slight conditions of depression, such as premonitions of early death, or in delusions of restraint and persecution, in other words, in the ideas which also are present in hysteria. In young girls who have not yet menstruated, therefore, in whom there is imperfect sexual development and hypoplasia of the reproductive organs, one occasionally encounters remarkable psychic changes, taciturnity, marked hysterical manifestations, bodily and mental hypersensitiveness, disturbances of nutrition, and frequently an obstinate and almost insuperable constipation. The disease conditions of the later period of youth, that is, from eight to sixteen years, have heretofore been insufficiently studied. The direction of an adequate interest to the age

of late childhood and beginning manhood is a service that still remains for pediatrics to render.

Pregnancy is undoubtedly to be regarded as a physiological process; indeed, in many ways it is accompanied by beneficial consequences both physical and mental. The healthy woman after a favorably terminated puerperium becomes younger; she appears fresher, more energetic, and more mature than the unmarried girl of corresponding years. Favorable sequels, however, are not the only ones which follow pregnancy. Especially in delicate young women of the refined classes one sees now and then that the months following delivery are attended by a rapid increase in weight, indeed corpulency, and a sense of increased health; but this gain, after perhaps half a year, is quickly lost. The increasing desire for food gives place to loss of appetite, the weight falls off markedly and is less than before the beginning of pregnancy, and hand-in-hand with this decreasing energy asserts itself, which stands out the more prominently if upon the young mother there fall greater household duties, social obligations, and the care of the child. Along with this reduction in weight and with the impairment of health goes a certain irritability, an inclination to capriciousness and to bad humor, of which the young wife herself becomes conscious, and against which she struggles vainly. All the signs of true neurasthenia and, indeed, overmastering impulses may develop.

Such a condition may, indeed, become unbearable, and often the husband desires a new pregnancy, in order to bring this state to an end. As a matter of fact, in the course of a new gestation the health and body weight are again restored, but this form of therapeutics is inefficient so far as permanency is concerned. After the second and, still more, after succeeding pregnancies the above-mentioned symptoms and loss of strength again appear in an aggravated form, usually not immediately after delivery, but months later. This time it requires longer rest, greater care, and more correct dieting, best carried out in a sanitarium, to combat the neurasthenia. "Neurasthenia," however, is not the correct designation for this symptom-complex. It is much more a general disturbance of nutrition and loss of strength, a condition which I desire to term post-puerperal asthenia of young wives.

So long as it does not reach an extreme degree, the vomiting of pregnancy is still to be considered a normal sign of pregnancy. To consider this vomiting as altogether hysterical would be to reverse matters, if we did not have to admit that hysterical vomiting also can occur in pregnancy. The uncontrollable vomiting of pregnancy is only a gradual increase of this manifestation of pregnancy. It differs from the uncontrollable vomiting of hysteria in that it is much more severe and that by it the stomach is emptied of its entire contents. Whereas, in the so-called uncontrollable vomiting of hysteria the general nutrition suffers surprisingly little, in the

severe form of the vomiting of pregnancy this is totally different. In the latter we see emaciation of extreme degree and complete exhaustion amounting to the condition of being absolutely bedridden; and the ferric chloride reaction in the urine shows us the severity of the inanition; so that usually, to avert death from starvation, an abortion must be resorted to.

If we do not regard the sporadic vomiting of pregnancy as hysterical, we are warranted in considering also its increased state, the uncontrollable vomiting, as not hysterical. As a matter of fact, in these cases the suggestion treatment usually proves itself ineffectual. As in the case of the physiological vomiting of pregnancy, one sees that the pernicious vomiting usually disappears quickly after the end of the third and fourth months. It is possible that it is associated with those processes of pregnancy which, during the third and fourth months, cease to make their baneful influences felt.

In a considerable number of cases of persistent vomiting still other diseased conditions, of psychic or somatic nature, occur. These are, perhaps, so seldom recognizable, because they are not at once apparent in prostrated and bedridden patients. Among these may be mentioned loss of the knee-jerk, marked weakness, and, later, atrophy of the hand and leg muscles, after the type of polyneuritic atrophy; further, disturbances of memory, conditions of excitement and stupor, and, indeed, even optic neuritis. This entire symptom-complex, expounded by Möbius and others, and repeatedly observed by me, corresponds absolutely to many toxic polyneuritides. Even as these do not limit themselves to a degeneration of the peripheral nerves, but may involve also the optic nerve, the brain, and the mind, so, in like manner may the polyneuritis of pregnancy, which latter, in the majority of cases, is associated with uncontrollable vomiting. If the disease picture is so severe that life is endangered and the premature interruption of pregnancy becomes necessary, one observes that with the removal of the produce of conception, after a time all the symptoms of the disease disappear, the patient awakes as from a sleep, and has sometimes no remembrance of the previous period of suffering, indeed of the pregnancy itself.

The neuritis of pregnancy is not always distributed throughout the entire body. At times it involves only an isolated area, as, for example, the perineal nerve. In such patients there may be some doubt as to whether the nerve plexus has not suffered through pressure of the pregnant uterus. In the severer cases of general polyneuritis, however, there can be no doubt as to the toxic nature of the affection.

Rudolph von Hösslin, to whom we are indebted for a valuable study of the nervous diseases of pregnancy, states that multiple sclerosis frequently develops during the course of pregnancy, and that often it becomes progressively worse with such succeeding pregnancy.

It has been remarked that this disease occurs more frequently in women than in men.

In this connection Pierre Marie has recognized that multiple sclerosis not infrequently appears in the course of typhoid fever. I have seen cases in which, after typhoid fever, there occurred the outspoken picture of polyneuritis, with optic neuritis and psychic disturbances. In one of my cases immediately after typhoid fever a symptom-complex developed which at first resembled polyneuritis, but later developed into typical multiple sclerosis with predominant spastic symptoms. It is well known that in the beginning of multiple sclerosis optic neuritis with swelling of the papilla is not infrequently present and that only later does this pass into atrophy. In consideration of these facts, it may be concluded that a relationship may exist between pregnancy and the neuritis of pregnancy, on the one hand, and multiple sclerosis, on the other, which we must explain in the same way as we do the association of typhoid neuritis and multiple sclerosis.

Let us turn now to the cardiac disturbances of pregnancy. These occur, as does the vomiting, in the first months of pregnancy, therefore at a time when one can scarcely speak of pressure of the uterus on the diaphragm and on the heart, or of mechanical interference to the circulation. These disturbances of the heart manifest themselves usually by extrasystolic arrhythmia, which gives rise to the uncomfortable sensation of intermittent heart action, to precordial flutterings and dyspnœa. They are improved by the use of alcohol and caffeine. If these symptoms become especially severe when in the recumbent position, they force the pregnant woman to sleep with the upper part of her body elevated. During the second half of pregnancy these heart and pulse irregularities may entirely disappear. They also tend to be absent in the interval between pregnancies. Once present, however, they recur with each new pregnancy; indeed, they can at such times be more severe and persist longer, even to the close of gestation. With the advent of labor they cease and give place to the slow regular pulse of parturition.

Of what character are the changes which give rise to the arrhythmia of pregnancy, I am unable to state, the more so since blood pressure determinations in such cases are wanting. They can have nothing to do with kidney disease, as in my cases no changes were observed in the urine. It is also improbable that they depend on serious myocardial changes, since they ordinarily tend to disappear with the termination of the pregnancy. One can conceive of reflex phenomena, transmitted through the nervous system. W. Müller has shown that the weight of the heart in pregnancy undergoes a certain increase, which approximately is proportionate to the general increase in the total body weight. This increase in the heart weight may be interpreted as evidence that during pregnancy the heart has greater work to do, greater resistance to overcome. Since

the extrasystolic forms of arrhythmia are to be regarded, for the most part, as an indication of a certain disproportion between the cardiac strength and the resistance to be overcome, we are, therefore, warranted in regarding these irregularities as an expression of an insufficient or not yet perfected adaptation of the heart to the increasing demands of pregnancy. After observing that subsequent to repeated pregnancies there sometimes occurs a persistent cardiac disturbance, especially arrhythmia, which, in the course of time, leads to the fully developed picture of heart-muscle insufficiency, we must conclude, unless a cause other than repeated pregnancies has been discovered for them, that sometimes the cardiac disturbances of pregnancy are responsible for permanent injury to the heart muscle.

Very frequently, in the course of pregnancy, the thyroid exhibits a moderately soft swelling, which, in the majority of cases disappears after the termination of pregnancy. Not infrequently, however, a struma remains. The enlargement of the thyroid in pregnancy is usually not associated with symptoms of hyperthyroidism. Indeed, to the contrary, if hyperthyroidism or even outspoken Basedow's disease exists before the beginning of pregnancy, during pregnancy these manifestations tend to diminish or entirely disappear. Apparently, therefore, pregnancy exerts a salient influence on hyperthyroidism. Only after a certain time succeeding the termination of pregnancy does it reappear more marked than before. Now and then one also sees that symptoms of hyperthyroidism develop for the first time several years previous to the menopause; that is, after women have gone through a series of labors and, as a consequence of pregnancy, present a thyroid enlargement, but no symptoms of hyperthyroidism. I believe it is not impossible that the remarkable variations in weight, that is, the general nutritional conditions, as well as the nervous conditions, which we may observe in association with delivery and the puerperium, are in some way related to the function of the thyroid gland. As exceptions to the rule that pregnancy favorably influences hyperthyroidism and Basedow's disease, now and then there occurs, in individual cases, an aggravation of the symptoms of exophthalmic goitre during pregnancy.

There exists in the life of males no parallel to the menopause of women. In men the sexual functions diminish much slower, and they disappear in perfectly normal men first at a great age or not at all. In women, to the contrary, the climacterium makes a very deep impression on life. The woman hitherto in vigorous health, within a short space of time is changed to a matron, and it is evident that such a change cannot take place without consequences to the bodily and mental condition.

The realization that old age is advancing can lead to mental depression; associated with this the bodily vigor becomes dis-

tinctly diminished, and much that life formerly held of work as well as of enjoyment must suddenly be largely relinquished. During the period marking the close of sexual life a condition of psychic depression often develops, which corresponds to that already noted in puberty. Women who until this time resolutely and happily met the duties of life and concerned themselves only with the welfare of their surroundings, become anxious and full of cares, see everything in a gloomy light, and bestow upon their own health an anxious attention which was formerly unknown. Often insomnia also appears and a certain restlessness. Likewise, complaints are often heard concerning failure of memory. This is referable more to the fact that women at this time first appreciate the physiological diminution of memory, while, as a matter of fact, memory and the powers of observation have been undergoing a gradual diminution for very many previous years. It is exactly the same as is the case in the gradual loss of accommodation power of the eye for near objects, which from childhood on progressively diminishes. The realization of old age, as also of failure of memory, comes when spectacles and the memorandum book become necessities. Between the above-mentioned mental changes at the menopause and the psychoses belonging to this period of life, all possible intermediate stages appear.

The tendency to corpulence at the climacterium is noteworthy; moreover, the accumulation of fat is characterized by a localization to parts of the body other than those affected during the time of fullest vigor. The figure changes to that of an old woman, but this is brought about less through a change in the osseous system, therefore, in the attitude of body, than through the accumulation of fatty tissue.

The changes in the heart and circulatory system are difficult to understand. It is a well-recognized fact that during the menopause many women begin to complain of heart trouble. Clément has described the "*cardiopathie de la menopause*," and Kisch also has called attention to it. There is seen, for the most part, a certain enlargement of the heart and a cardiac arrhythmia of the type of the extrasystole. Extrasystolic arrhythmias are frequently the sign of an inequality between the strength of the heart and the resistance to be overcome. An examination of the blood pressure frequently showed me in such cases a hypertension such as we should scarcely expect in women. Readings of 180 to 200 mm. of mercury (Riva-Rocci apparatus) are not at all unusual in such cases. We will hardly err if we ascribe this elevated blood pressure to arteriosclerotic processes. Arteriosclerosis of women may, for the most part, be attributed to causes other than is that of men. It seems much more frequent in women who have had children, and especially in those who have brought children into the world a number of times, than in unmarried or sterile women. Probably it has a certain relationship to the cardiovascular conditions of pregnancy

already referred to. The cardiac disturbances of the climacterium, which can finally develop the picture of severe heart-muscle insufficiency, occur certainly much more often in fat than in thin women, and the functional weakness of the heart has a certain relation to the general loss of muscular power, which in the corpulent generally can attain a high grade, but does so especially in fat women at the time of the menopause.

While the process of the menopause under normal conditions occupies a period of from one to three years, it may occur very quickly if disease of the sexual apparatus makes the complete operative removal of the ovaries necessary. In this postoperative "*climacterium præcox*" we see all the characteristic appearances of the menopause occur much more violently: the congestions of the head and other vasomotor signs, palpitation of the heart, the tendency to fat deposits leading to the characteristic posture of the old woman's figure, the loss of physical and mental energy, and above all the signs of psychic disturbances and depression.

I have seen several cases in which total extirpation of the reproductive organs during the twentieth or thirtieth year produced extraordinary consequences on the mentality and the entire personality, and blighted blooming, promising careers. Careful operators, in order to lessen the unfavorable results of the "*climacterium præcox*," seek to leave behind a small piece of the ovary. Removal of the uterus alone seems not to call forth these severe sequels, but a number of my cases seem to indicate that the untoward results reach an especially high grade when, in addition to the ovaries, the uterus is totally removed.

It is well known that a sterile marriage can bring with it serious mental disturbances to the wife. Indeed, this concerns not only those women in whom sterility has occurred through disease of the uterus and adnexa, but also in those in whom the cause of the sterility is to be sought in the person of the husband. Finally, it also holds true for the women with underdeveloped uterus and sexual organs, who often are conspicuously slender and tall, and whose pelves resemble more the type of the male pelvis. If, in the sterile woman, the desire for a child is very keen, the occurrence of every menstruation brings a new disappointment, and each accidental delay of the period arouses a false hope whose unfulfilment is then that much more disappointing. This continual change between hope and disillusionment not infrequently results in a shattering of the psychic well-being, which at first expresses itself in abnormal susceptibility and irritability, but finally in all the possible symptoms of hysteria. When the husband, as so frequently happens in sterile marriages, regards his wife with particular affection, there then often develops a condition of affairs in which the wife seems like the child, indeed, the spoiled child, of the husband. Only when the menopause banishes the last hope of issue comes peace.



II. Diseases of the female reproductive organs can give rise in the most varied ways to pathological processes in other internal organs. I shall not at this time touch upon their relation to the nervous system, and hysteria in particular, a theme which has been discussed many times and of which our conception has undergone many changes.

Disturbances of the function of the bowels are to be mentioned among the most frequent sequels of diseases of the uterus and adnexa. Constipation is the rule. It may be caused mechanically, but is also often encountered when pressure on the sigmoid or rectum does not exist. Further, this constipation can give rise to a whole train of resulting symptoms.

We see especially frequently mucous colitis in association with diseases of the reproductive organs. Typical mucous colitis is a condition which belongs almost exclusively to the female sex. Indeed, it is found chiefly in those women who present a neuropathic tendency and the most varied symptoms of a nervous character. Those who carefully investigate these cases will be surprised how frequently diseases of the uterus and adnexa may be recognized with it. It is hardly possible to give an explanation for this relationship. All cases of mucous colitis are certainly not to be brought into etiological relationship with the reproductive organs. Many of them may occur as the result of constitutional anomaly, by means of abnormal mucous secretion and spasm of non-striated muscular fibers, just as bronchial asthma, which is characterized by an excessive migration of the eosinophilic leukocytes to the diseased mucous membrane.

We see that myoma of the uterus is accompanied, with exceptional frequency, by evidences of disease in other organs. The danger attendant upon the "myoma heart" was first recognized by the surgeons. In these cases, in which, after a successful myomectomy, sudden heart failure occurs, there is usually found a markedly soft and flabby heart. This condition of the heart muscle must be regarded as the result of frequent and profuse uterine hemorrhages. During life, however, disturbances of cardiac action are also observed in those cases of myoma in which the loss of blood throughout has not been excessive, and in which the blood examination itself reveals no noteworthy impoverishment of the blood corpuscles and hemoglobin. The relation of myomas to the diseased condition of the myocardium cannot be explained by the anemia alone. Furthermore, the mechanical pressure of the uterine tumor cannot be held responsible for this condition. To give a satisfactory explanation of the relation between myomas and heart disease is at present impossible.

The relation between myomas and goitre is equally obscure. For a physician whose field of activity lies in a goitre country it is naturally difficult to say whether this relationship is only accidental,

or whether it can also be claimed as applying to other lands. However, it has also been noticed by other authors, as for example by H. W. Freud and Fischer. In Munich it is so common that I have made it a rule to examine all women with thyroid enlargement for myomas, and vice versa.

The outspoken picture of hyperthyroidism is often associated with abnormal enlargement of the heart and a quickened irregular pulse. Therefore, in a considerable number of cases it is difficult to decide whether it is better first to operate upon the goitre or the myoma, or whether, in consequence of the danger from the struma and heart, a myomectomy should be permitted at all. From the experience of gynecologists it has been repeatedly proved that a myomectomy exercises a favorable influence upon both the heart and the thyroid.

One also sees, now and then, that disease of the adnexa can give rise to disturbances of the heart. I have seen cases of severe gonorrhoeal pelvic inflammation in which there has occurred, almost regularly with every menstruation, arrhythmia of the heart, excessive rapidity of the pulse, and even true delirium cordis. These women, at their menstrual periods, find themselves in a condition of pitiable cardiac weakness, which is only slightly influenced by strychnine and heart stimulants. With improvement in the diseased condition of the adnexa, or with the advent of the climacterium, this condition may completely disappear.

The frequent relationship between disease of the adnexa, as well as inflammation and adhesions in small pelvis, to the nervous system is well known. Let me caution you that the resulting pain, weakness, and paralysis of the lower half of the body is always to be regarded as reflex or as functional. A thorough examination often reveals that, due to inflammation and adhesions in the pelvis, there has occurred an injury, a pressure palsy, or a neuritis of the nerves passing through the pelvis. For the woman whose constant complaints have been regarded as hysterical and been looked upon with indifference, it is always a real satisfaction when the establishment of an organic lesion furnishes a certain amount of justification.

The relationship of gynecological diseases to the organic diseases of the peripheral nerves and central nervous system has also been admirably considered by Rudolph von Höslin.

III. We now come to the diseases of other organs in which a certain relationship to the female reproductive organs is recognizable. In this connection first to be mentioned are diseases of the kidneys and urinary tract.

The relationship of kidney disease, in its strict sense, to the female sexual organs may be twofold. In the first place, pregnancy can lead to the kidney of pregnancy. The latter is found in the vast majority of all cases of eclampsia; at all events it stands in the closest

relation to it, even if eclampsia may not be considered as alone the result of the kidney of pregnancy.

The high albumin content and the large number of casts which may be observed in this disease prove that a severe affection of the kidney tissue exists. The macroscopic appearance of the kidney, with the high grade of fatty degeneration of the parenchyma also warrants this interpretation. However, the microscopic examination proves that the epithelium, in spite of the marked infiltration with fat droplets, has undergone no true necrosis, that the nuclei are preserved, and that the glomeruli show no change worthy of mention.

The clinical course shows that a quick recovery is established soon after the discharge of the product of conception, and that after a few days the urine may show a completely normal condition. The lesions of the kidney tissue, notwithstanding the striking associated phenomena, are not of a serious nature, or, at least, are amenable to quick repair. Nevertheless, to conclude, from the microscopic appearance of stained preparations, that the functional disturbance of the kidney of pregnancy is unimportant, is at variance with the suppression of urine at the height of the disease and with the severity of the symptoms and the danger to life, as well as with the frequency with which a premature termination of pregnancy occurs. Unfortunately, I do not know how the blood pressure acts in the nephritis of pregnancy and in eclampsia.

The kidney of pregnancy has been rightly considered the result of an intoxication from the foetal site. However, it is yet to be determined whether the products of the metabolism of the child or a syncytiotoxin furnish the cause.

On the other hand, pregnancy can occur in a woman who previously has suffered with nephritis. The nephritis may light up in the course of the pregnancy, and, indeed, this is the rule. Uremia may occur, which is with difficulty distinguished from eclampsia, and thereby may threaten the life of the mother. In such cases, in which the maternal life is preserved, it now and then becomes manifest that, as a result of pregnancy, the nephritis has suffered a further and permanent aggravation.

Pregnancy, however, by no means always exerts such an unfavorable and dangerous influence on a preëxisting nephritis, and the danger of uremia or eclampsia is in no way so great as many suppose. It is not unusual for a woman who has chronic nephritis to undergo many pregnancies without special harm, but the life of the child in all these cases is in the greatest danger. The product of conception almost always, sooner or later, dies and is discharged. The majority of nephritic women experience the misfortune that in spite of repeated conceptions they are unable to bring a living child into the world, a fact which seems to warrant prohibition of marriage in chronic nephritics. The inability of the kidneys completely to eliminate from the body the waste products of metabolism seems more dangerous to the child than to the mother.

It is recognized that inflammation of the bladder, and especially of the pelvis of the kidney, is extremely frequent as the result of pregnancy and disease of the female reproductive organs. Indeed, it is often the difficulty in emptying the bladder which, through the resulting retention, induces undue distention of the bladder, ureters, and pelves of the kidneys, that favors infection. As a rule, we see that a bacterial infection can very easily take place, especially at that place where stasis of the secretions occurs. This applies to the urinary tract as well as to the stomach, the intestines, the gall-bladder, and the bronchi. The bacterial infection of the bladder, the ureters, and the pelves of the kidneys in many cases certainly occurs from the urethra. In support of this, facts indicate that in woman cystitis and pyelitis occur disproportionately more frequently than in man, whose urethra is longer and whose bladder is more tightly closed.

However, the possibility must also be reckoned with that infection of the urinary tract can also occur directly from the adjacent intestines and through the blood and lymph. In support of this possibility is the fact that in many cases the pelvis of the kidney apparently is first involved and that the bladder shares secondarily in the inflammation. Further, it is to be observed that these pyelitides and cystitides show with overwhelming frequency, as the single infectious agent, *Bacillus coli communis*, the normal occupant of the intestinal mucosa. Also in other cases, in which later *Proteus vulgaris*, the causative factor of ammoniacal urine fermentation, or other bacteria are found, the presence of *Bacillus coli communis* is often established first.

Finally, pyelitis occurs chiefly in those individuals who suffer from obstinate constipation. It has been shown that in stagnation of the intestinal contents the bowel wall becomes permeable for bacteria. From the relationship between constipation and pyelitis it follows that the therapy of pyelitis only offers the prospect of success when it is efficient in overcoming the constipation.

The pyelitis begins for the most part acutely, with sharp pain on the side of the affected kidney, and usually with considerable fever. The urine is often bloody and shows almost constantly, by a considerable quantity of albumin and casts, that the kidney is involved. The number of bacteria in the urine is very great. A number of bacteria present in urine removed from a sterile bladder need not always be the sign of a cystitis or pyelitis. As is well known, this occurs in infectious diseases due to bacteria of various kinds and from various parts of the body, in erysipelas, angina, endocarditis, typhoid fever, mastitis, and phlegmons, and sometimes from the secretion of the infectious agent through the kidney. But, this excretion of bacteria through the urine does not tend to produce inflammatory changes in the urinary tract. It does not lead to an increased number of leukocytes in the urine and purulent cloudiness of the urine,

and commonly disappears within a short time. As opposed to this bacterial excretion in infectious diseases, the bacterial infection in pyelitis proves to be extraordinarily obstinate. It withstands all antiseptics, even urotropin, and I have yet to see the urine after pyelitis become absolutely bacteria-free. The inflammatory phenomena, however, the albumin and leukocytes in the urine diminish in the course of a few weeks after careful treatment, and finally the picture of chronic bacteremia results. In that condition bacteria, indeed, especially the colon bacilli, are still present in numbers, but give no more indications of the signs of inflammation in the region of the pelves of the kidneys or bladder. There must be established a form of tolerance or immunization of the mucous membrane to the particular bacteria.

If, however, in such cases, there occurs at any time an obstruction along the urinary tract, the inflammatory processes soon flare up again; once more pain, fever, and marked leukocytosis occur, and the urine again shows a sediment of pus. It is for this reason that during pregnancy, in chronic infection of the urinary system, there is always the danger of again lighting up a pyelitis, and the damming up of pus in the pelvis of the kidney leads to pyonephrosis. Pregnancy, therefore, can give rise, through stagnation along the urinary tract and through constipation, not only to the primary origin of infectious pyelitis, but it may also induce a recurrence of the process in an already infected urinary tract. Pus in the renal pelvis during gestation may lead to quite serious symptoms and protracted febrile conditions. In many cases the condition becomes so serious that assistance of an operative nature must be sought.

Opening of the renal pelvis, for example in pyonephrosis, leads to a continuous discharge of pus from the wound, and intolerable annoyances from such a fistulous formation result. An extirpation of the kidney itself is only justified in those cases in which the entire kidney is destroyed by pus and when the other kidney is healthy. One will not lightly decide upon this operation. It is much more preferable to terminate pregnancy and save the life of the mother.

In the pyonephrosis of pregnancy the prognosis is favorable in so much as the obstruction is produced by a process of transitory nature. One can see the end and, in imminent danger, at any time terminate pregnancy. The prognosis of urine stagnation is worse in many gynecological diseases, in which neoplasms and dense adhesions in the pelvis produce compression of one or both ureters. In such cases, should an infection of the pelvis of the kidney occur, thus leading to pyonephrosis, in many cases nothing can be done but extirpation of the kidney, provided the process is unilateral.

If, on the other hand, ureteral compression involves both sides, the woman will lapse into a chronic illness, and after marked

febrile manifestations will finally succumb with uremia. It has been denied that blocking of the ureters can lead to true uremia. As a matter of fact, one sees that an acute blocking of both ureters usually does not produce the typical picture of uremia; the patients succumb rather to a progressive asthenia, as Ascoli especially has emphasized. In chronic ureteral constrictions, on the other hand, one notes, in the course of time, typical blood pressure elevations up to 180 to 200 mm.; indeed, as I once saw, up as far as 300 mm. mercury. Hypertrophy of the left and also of the right ventricle may be recognized; headache, vomiting, and, indeed, severe uremic attacks may be observed. Only a longer time is necessary to bring these uremic conditions to full development. In one such case, in which both ureters were compressed by a malignant growth of the uterus and bilateral hydronephrosis existed, I could establish, in association with a considerable blood-pressure elevation recognizable during life, an hypertrophy of the left ventricle, as shown by post-mortem examination. The kidney tissue was involved to a marked degree, there was present a slight increase, and here and there also a certain infiltration, of the interstitial tissue. The uriniferous tubules were compressed and displaced as a result of the pressure of the hydronephrosis, but a vast majority of the glomeruli showed no change. This case proves that blood pressure elevation and heart hypertrophy can occur without any essential anatomical damage to the glomeruli.

In case of an infectious pyelitis, the pelvis of the kidney is infected by inflammation-producing organisms; therefore this process is never unimportant for the kidney itself. Indeed, only in the first acute beginning of such a pyelitis does the urine tend to contain a large amount of albumin, casts, and blood casts in greater numbers. The blood pressure in acute pyelitis always remains normal. If, however, the pyelitis lasts a year, not infrequently the albumin content gradually again becomes greater than corresponds to the coincidently diminishing suppuration. Vascular hypertension and hypertrophy of the heart gradually develop, and finally, the picture of a chronically progressing contracted kidney results.

Fieder has described a symptom-complex, designated by him, as ovulation fever (*Ovulationsfieber*), in which at the time of menstruation, there appear a fever of short duration, sometimes slight and sometimes again high. I, too, have seen such cases: women, who in the interim give the impression of complete health, become ill at the time of menstruation, with febrile phenomena of considerable intensity. They have complete loss of appetite and coated tongue, with decidedly marked constitutional symptoms, and a certain pain may be elicited by pressure above the symphysis. Sometimes such febrile movements occur exactly midway between two menstruations, at the time when many women feel the so-called middle pain (*Mittelschmerz*). The association of these febrile movements of

only two or three days duration with menstruation was unmistakable. Concerning this, it has been thought that this ovulation fever is the result of the physiological incident of the ruptured follicle in the ovary and the associated phenomena of hyperemia. I prefer to consider that these febrile manifestations occur only in those cases in which a latent disease of the genitalia previously exists, which either depends upon a gonorrhœal basis, or exists in connection with some other form of infection, for example, puerperal infection. I surmise that through hyperemia incident to menstruation this latent focus of infection again lights up. The tenderness above the symphysis or slight pain and swelling of the adnexa seems to me to confirm this explanation. Upon more careful examination my cases showed that there was present every time a chronic infection of the urinary tract, as a pyelitis, and this, indeed, acted like an infection by either colon bacilli or proteus. It could also be established that at the time of the attacks of fever a spontaneous lumbar pain was sometimes complained of, or that bimanual palpation of the kidney region caused pain. Although I do not entirely ignore the first-mentioned possibility, it seems that the last-named observation points to the fact that a pyelitis underlies many cases of ovulation fever, and that this pyelitis, in connection with menstruation, undergoes an aggravation similar to that which has already been considered in connection with pregnancy. Whether menstrual processes can really lead to fever and the phenomena of sickness, if the genital organs and the urinary tract are absolutely normal and free from infection, I must leave to the gynecologists to determine.

The bile passages show relations to the female reproductive organs quite like those we have discussed in connection with the urinary tract. It is recognized that cholangitis, cholecystitis, and gallstones occur three to five times more frequently in women than in men. It is certain that intestinal sluggishness is responsible above everything else for the conditions of congestion and infection of the biliary tract. This is perhaps the reason why we find gallstone colic in association with diseases of the female genitalia.

Above all else, pregnancy is undeniably associated with gallstones. I have repeatedly seen gallstone conditions in pregnant women and still more frequently in the course of the puerperium and in the succeeding weeks. Many times patients have come to me, in whom during the course of the puerperium an attack of fever and severe abdominal pain have given rise to the suspicion of a puerperal infection, but in which the further course of the disease—localization of the pain to the region of the gall-bladder radiating to the right shoulder, as well as the occurrence of slight jaundice, and a distinct urobilin reaction in the urine—made certain the diagnosis of gall-bladder disease. If one elicits accurate histories from women who for years have suffered with gallstone colic, in many cases he can convince himself that the first attack of colic, which usually was first

regarded as pain in the stomach, occurred in these people after a puerperium. Married women who have had many children are, at all events, much more frequently the subjects of gallstones than the unmarried.

Appendicitis also has a relationship to diseases of the female genital tract. I have repeatedly seen acute appendicitis, the initial attack as well as recurrences, occur at the time of menstruation. It is often difficult to differentiate between appendicitis and an acute inflammation of the adnexa. Often in an outspoken appendicitis the adnexa show a certain participation, since they appear to be the seat of inflammatory swelling and pain. In the further course of the disease the adnexa may be pulled up and fixed by means of adhesions with the inflammatory process in the appendix. In disease of the adnexa in combination with appendicitis one rarely makes a mistake if the appendicitis be regarded as primary and is treated as such. If appendicitis has existed and has left relics behind, with every menstrual period a fresh attack of pain may occur. Pregnancy may also influence detrimentally an incompletely healed appendicitis. I remember one case in which continued appendiceal pain led to an examination of the pelvic organs, whereupon the presence of beginning pregnancy was proved. In those cases in which the appendix has been removed because of appendicitis, inflammations, adhesions, stitch and stump abscesses of the female reproductive organs may occur in sympathy, or disease of the adnexa and painful pregnancy may be produced at the site of the old operative scar.

Just as the appendix is, so also may the pelvic organs be sympathetically involved by inflammation which originates at the sigmoid. Sigmoiditis and perisigmoiditis are by no means as rare as was formerly believed. They stand in etiological relationship to many cases with persistent constipation, and the resulting adhesions may give rise to kinks of the intestines, obstinate constipation, and indeed to ileus. Perisigmoid adhesions may claim as their sequels dragging on the bladder, pain upon overfilling of the bladder, as well as displacements of the uterus and adnexa. It has been shown that sometimes chronic constipation may give rise to inflammatory conditions in Douglas' pouch, and thereby to disturbances in the female genital area. This periproctitis, which, however, is caused not only by chronic obstruction, but also by all sorts of other diseased conditions of the lowest part of the bowel, stands in the closest relation to perisigmoiditis.

It still remains, however, to take up the relation of the female genital organs to the constitutional and infectious diseases, but out of this vast field only two chief headings shall be dealt with—diabetes and tuberculosis. It is the rule that pregnancy and the puerperium are excessively fatal in diabetic women. I have seen and observed exceptions to this rule, that is, that women, who suffered with well-



marked glycosuria have passed through several labors without injury to their health. Such observations, however, must not mislead one from the principle that in the presence of diabetes marriage must be urgently opposed.

As in many other infectious diseases, for example, typhoid fever, smallpox, and pneumonia, it follows in tuberculosis that pregnancy and the puerperium exert in general a deleterious influence. A previously latent or at least favorably progressing tuberculosis may during the course of pregnancy experience a rapid spread and aggravation, and not infrequently in the course of the puerperium a fatal termination occurs. I have never observed that pregnancy had a favorable influence on tuberculosis, as has been stated by some physicians. The unfavorable effect which pregnancy, as a rule, exercises on tuberculosis is one of the most significant examples of the importance of predisposition, that is, of the general state of nutrition, in the development of this disease. Indeed, here it is an acquired and temporary alteration in the nutrition of the organism that smooths the way for an acute increase of the disease.

The numerous observations which we make concerning the influence of pregnancy on tuberculosis obligate every conscientious physician to oppose most earnestly the marriage of girls suffering with tuberculosis. But what is the result of this medical advice? Of the many young women with incipient tuberculosis who have consulted me in regard to the advisability of getting married, and whom I always most emphatically warned against it, *all* have married, and, with a single exception, all have died within a few years. This exception became pregnant on her wedding journey, and shortly thereafter had a severe hemoptysis. An induced abortion brought the fever and the spread of the disease to a standstill. Not only in this, but in many other cases of beginning tuberculosis, have I seen an early interruption of pregnancy favorably influence the further course of the disease.

The foregoing explanations may, notwithstanding their incompleteness, afford a picture of how numerous are the relations between internal medicine and diseased conditions in the female reproductive organs. They should emphasize how important it is for the internist, and especially for the general practitioner, to turn his attention to the gynecological condition, and in suitable cases to seek the advice of the gynecologist. On the other hand, with justice we can expect the gynecologists to direct their attention, more than they have heretofore, to medical disorders, and in doubtful cases to secure the advice of the internist.

**THE SPECIFIC TREATMENT OF TYPHOID FEVER.**

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It is the purpose of this paper to discuss general principles rather than to go into details. I wish to inquire into the probabilities of the discovery of a specific treatment for typhoid fever and what the nature of such treatment is likely to be, and how much we may expect from it. It seems to me that enough has been done to convince us that no antitoxin, comparable to that which we have for the treatment of diphtheria, is likely to be found for typhoid fever. Diphtheria is so essentially different from typhoid fever in the nature of the infection that to draw conclusions from the one and try to apply them to the other seems wholly without warrant. In the former the bacillus grows on a mucous surface, developing a chemical poison which is absorbed into the circulation and which induces the systemic symptoms of the disease and causes death. In typhoid fever the bacillus first finds its way into the interior of the body and finally into the blood. One is, strictly speaking, apart from its local action, an intoxication; the other is a true systemic infection. In diphtheria the bacillus is the producer of the poison; in typhoid fever the bacillus is the poison. The poison of diphtheria reaches the blood as a soluble, chemical body; the poison of typhoid fever reaches the blood as a living, multiplying cell. The poison of diphtheria is a soluble toxin; that of typhoid fever is an integral part of the bacterial cell, and if our definition of a toxin is a poison that may be used to generate an antibody to itself, the active agent in the typhoid bacillus is not a toxin, because there is not the slightest evidence that in any animal it elaborates an antibody.

There is no satisfactory evidence that the typhoid bacillus produces a soluble poison. It may be true, as has been asserted by some, that old cultures of the typhoid bacillus, after the removal of the bacterial cells by filtration through porcelain, are slightly poisonous, but any feeble action that may be shown by such filtrates is easily accounted for by the autolytic changes that go on slowly in all cells and, in fact, in all organic matter. No one has ever been able to produce an antibody by treating animals with such filtrates or any other culture of the typhoid bacillus, living or dead, young or old, filtered or unfiltered.

It seems to me that the time has come for us to recognize that the mechanism of immunity is not the same in all infections and intoxications. I think that there is already sufficient ground to justify us in holding that there are at least three forms of immunity, and these I will briefly designate as follows: (1) *Antitoxin Immunity*. The poisons to which this form of immunity has been secured

are the venom of serpents, vegetable poisons, such as ricin and abrin, and the toxins of *Bacillus diphtheriæ*, *Bacillus tetani*, and *Bacillus botulinus*; possibly others may be added to the list in the future. These poisons apparently constitute a distinct group, and they resemble enzymes in the following striking particulars: (a) in aqueous solution they are destroyed by a temperature of 100° or less; (b) they are active in solutions so dilute that they do not respond to the three most characteristic proteid color reactions, the biuret, Millon, and Molisch tests; (c) animals treated with successive doses at proper intervals develop antibodies; (d) their effects are not immediately manifest, but develop only after a period of time. For the present, at least, Ehrlich's side-chain theory must be regarded as the most satisfactory explanation of this form of immunity. There is no proof so far that either phagocytic activity or proteid cleavage has any concern in the production of this form of immunity.

(2) *Phagocytic Immunity*. This form of immunity has been best studied with the cocci, and it has been shown experimentally that with virulent or slightly virulent strains phagocytic activity may be markedly increased, but that with highly virulent strains it is difficult to demonstrate increased efficiency in the destruction of bacteria by the phagocytes.

(3) *Lytic Immunity*. This is frequently designated as bactericidal or bacteriolytic immunity, but there are the following grave objections to the employment of either of these terms: (a) bacterial proteids are not the only proteids that may be, and are, split up in the animal body. Most foreign proteids, when introduced directly into the circulation and without previous subjection to the digestive juices, undergo specific proteolysis, and this is true whether these proteids are living or dead. (b) The cleavage of poisons in the body is probably not confined to those of proteid composition. (c) The term bactericidal is inappropriate, because the bacteria may be so altered chemically that they are robbed in part or wholly of their harmful properties, and still are not killed. Examples of the persistence of specific bacteria in the body after recovery from the disease are well known, and immunity to disease may co-exist with the specific bacterium of that disease still living in the body. The bacterial proteid owes its poisonous action to its molecular structure, and this may be so modified as to render the organism a comparatively harmless guest without destroying its life. (d) The term bacteriolysis is certainly inappropriate, first, because all these poisons are not bacteria, and the term implies that the bacterial cell is destroyed; and we have just seen that this does not happen in all cases. In view of the facts here briefly considered, I prefer the word "lytic" to designate this form of immunity; however, I am not altogether satisfied with this term, and hope that some one will soon suggest a better.

There is no antitoxin for the typhoid poison; phagocytic action certainly is not a marked factor in the natural recovery from this

disease, and it is my purpose to see what we can make out of lytic action in the study of the nature, progress, and recession of typhoid fever.

It is probable that in some diseases two of these immunizing or protective factors may combine in aiding the animal body in its contest with infection. This seems to be the case in tuberculosis, for instance, in which phagocytic and lytic immunity both are concerned, with the latter playing the more important role. Future studies may show a closer relation between phagocytic and lytic protection than can be demonstrated at present, but both of these differ so radically from antitoxin immunity that to try to explain them by the same theory seems to be without justification. Such passive immunity as we secure when we treat a diphtheritic child with specific antitoxic serum is wholly without any parallel in typhoid fever, colon infection, tuberculosis, or pneumonia. In the former the cellular activities of the child are not awakened at all; its circulatory system may be compared to a large, branched test-tube, into one arm of which the toxin produced by the bacillus growing in the pharynx is poured, while into another arm the antibody or neutralizing agent is introduced. In short, the treatment of diphtheria with the antitoxin is in essence an experiment *in vitro*, with only this difference, that if the poison is not neutralized by the antidote promptly it may act upon certain cells in the child's body and may cause death, and just to the extent that it is not neutralized it does cause sickness. In the other diseases mentioned there is no such soluble poison, and we possess no such antidote. The poison is a particulate, living multiplying cell, and it can be destroyed only through the activity of the body cells, and when the invading cell is destroyed its poisonous constituent can be neutralized only through the activity of the body cells.

For some years my students and I have been engaged in the study of the so-called endotoxins, or, as I prefer to designate them, the proteid poisons. We have shown that all the true proteids with which we have worked can be split by chemical agents into poisonous and non-poisonous groups. We have been able to accomplish this by extracting the proteid body at 78° with a 2 per cent. solution of sodium hydroxide in absolute alcohol. This causes slow hydrolysis, by means of which cleavage of the proteid molecule is secured. When the process is properly carried out the separation of the poisonous and non-poisonous constituents is fairly satisfactory. The method is certainly crude compared with the like process as it takes place in the animal body, and, as we have elsewhere stated, much of the poisonous group is destroyed by our method, but there is enough left to enable us to investigate its properties. The proteid molecule, whether it be of egg-white or of the typhoid bacillus, is made up of groups, consisting for the most part of the mono-amino and di-amino acids, combined with one another, with phosphorus,

and with carbohydrate. The exact manner of these combinations, even in the simplest proteids, is not yet known. We have obtained the cellular substance of the typhoid bacillus and of other bacteria in large amount, and have shown by splitting them up that they are, in their essential parts at least, true proteids, just as much so as are egg albumin and serum globulin. For our present purpose it is well to regard the typhoid bacillus as a living proteid, capable of growth and multiplication, but chemically nothing more than a proteid.

It will be best to state briefly some of the properties of the products obtained by splitting up the proteid molecule with dilute sodium hydroxide in absolute alcohol. As has been stated, this method breaks the complex body into two simpler parts, one of which contains all the poison. The poisonous portion is freely soluble in absolute alcohol, while the non-poisonous portion is wholly insoluble in this menstruum. Indeed, this is the chief reason for using an alcoholic rather than an aqueous solution of dilute alkali in effecting the cleavage. When water is used as the menstruum, both portions being soluble in this, separation is obtained with difficulty and imperfectly. That the cleavage has followed a definite line in the molecular structure is shown by the following: (a) the poison contains no phosphorus, (b) the poison contains no carbohydrate, and (c) the poison contains the greater part of the aromatic radical. These facts show that the separation is a chemical one, a true molecular cleavage, and not a mere disintegration. The splitting process has followed a definite structural line; otherwise, the phosphorus and the carbohydrate could not all be in one of the products. In other words, the cleavage is such as one might expect to obtain by the action of a ferment. If it be objected that I have no right to compare the effect of so gross an agent as an alcoholic solution of sodium hydroxide with so delicate a one as an enzyme, I need only inquire in return whether or not there is any difference between the tyrosin obtained by the digestion of meat with the pancreatic juice and that obtained from the same meat by splitting it up with 30 per cent. sulphuric acid? Besides, the trypsin acts at the temperature of the animal body, while the meat is boiled for hours with 30 per cent. sulphuric acid, and yet both processes yield the same tyrosin. Compared with the sulphuric acid used in preparing tyrosin, our dilute solution of sodium hydroxide in absolute alcohol is mild indeed. It is characteristic of ferments that they induce at relatively low temperatures chemical reactions that can otherwise be brought about only with powerful chemicals at relatively high temperatures. Chemists are fond of comparing the complicated structure of the proteid molecule to that of a house of cards, and this is a fit comparison. Now, when the house of cards is blown down, whether it be by the breath of the child that has built it or by a blast of wind, it is blown into cards in each case—nothing more. The greater force

may scatter the cards more widely, and it may even twist and tear some of the individual cards, but, on the whole, the house is broken up into its constituent parts whether the disrupting force be the breath of the child or a blast of wind. I dwell upon this point because I shall attempt later to show that by our method we have split up the typhoid bacillus, obtaining not only the true endotoxin, but its specific antigen. Quantitatively I not only admit, but I know, that our method is crude, and that the amount of poison obtained from a given number of bacilli is less than that liberated in the animal body, but qualitatively the results are the same.

If we are to study typhoid fever satisfactorily, it will be necessary to go into some detail concerning the products obtained by cleavage of the cellular substance of the typhoid bacillus. In the first place, I will briefly state the method of obtaining typhoid bacilli in large amount. This organism is grown in incubating tanks 10 feet long and 2 feet wide, and with six of these tanks in operation we are able to obtain abundant growths. When the growths have reached maturity they are detached from the subjacent agar, drawn into proper receivers, washed with physiological salt solution, then placed in Soxhlet's apparatus and thoroughly extracted first with alcohol and then with ether. The germ substance thus obtained is finely ground, passed through a fine-meshed sieve, then split up with the alcoholic solution of sodium hydroxide, as already stated.

The poisonous portion is freely soluble in alcohol and in water, more freely in the former than in the latter. It is also soluble in methylic alcohol, but is insoluble in chloroform, benzene, and ether. From its alcoholic solution it is precipitated by ether. Its aqueous solutions respond to the biuret and Millon tests for proteids, and at present we must regard the poison as still a proteid, but, of course, of much simpler structure than the bacterial substance from which it has been obtained. When the poison is split up with 30 per cent. sulphuric acid it yields mono-amino and di-amino acids, tyrosin being present in large amounts. The poisonous action of this body is probably due to the aromatic radical which it contains so abundantly, and to which its ready response to the Millon test is due. So far we have split up some twenty-five proteid bodies, bacterial, vegetable, and animal, and we have found no true proteid that has not yielded a poisonous group. The albuminoid gelatin contains no poison, and it contains no aromatic group, or contains such a group only in minute trace, as is shown by its failure to respond to the Millon test. This is additional proof that the aromatic radical constitutes the poisonous group, or is contained in it. In this connection, Wells<sup>1</sup> has found that animals are not sensitized by gelatin as they are by the true proteids. This is what we should expect, since gelatin does not contain a poisonous group. As Wheeler and

<sup>1</sup> Jour. Amer. Med. Assoc., February 15, 1908.

I have found, and as has been confirmed by Nicolle and Abt,<sup>2</sup> Witte's pepton does contain a poison, but the French scientists have found that Defresne's pepton does not. It would be interesting to know whether the latter is made from gelatin or from a true proteid.

The effect of the isolated typhoid poison on animals is identical with that of any other proteid poison. While the proteid poisons are probably not identical chemically, they are identical in their effects upon animals, and if the white of egg could be introduced into the blood and could grow or increase in amount after its introduction, it would cause disease and death much as the typhoid bacillus does. The latter is a living, growing, multiplying proteid, and it is because it can live, grow, and multiply in the body of man that it is able to induce disease.

The effect on animals of the free poison obtained by splitting up the typhoid bacillus after the manner stated is of much interest. It is the same as that of all the proteid poisons with which we have worked, and I believe that in certain diseases, notably in colon and typhoid infection and in tuberculosis, possibly in many other diseases as well, the poison is practically the same. The specificity of these diseases does not lie in the poisons produced in them, but in the non-poisonous constituents of their respective bacteria. When the free typhoid poison is administered to a rabbit or guinea-pig by the mouth there is no recognizable effect. This may be due either to destruction of the poison by the digestive juices, or to the slowness with which it is absorbed. When the poison is introduced into a collodion sac and this is placed in the abdominal cavity of a rabbit, there is no detectable effect. In this case the failure to induce reaction is best explained by the slowness with which the poison is absorbed, the comparative insusceptibility of the animal, and the difficulty that we have of recognizing anything but relatively abrupt effects upon animals. That man is much more susceptible to this poison than laboratory animals is shown by the fact that when we rub up the crude typhoid poison in a mortar, if the mouth and nose of the operator be not protected by a mask, the operator has frequently shown evidence of poisoning. The first thing noticed is an irritation of the nasal mucous membrane and a huskiness of the voice; this is followed by a feeling of depression and malaise, with chilly sensations, after which the temperature has been found as high as 102°. Rarely nausea and vomiting have resulted. After a period of discomfort of from six to ten hours, with pain in the joints, complete recovery follows.

When a fatal dose of the free poison is administered to a guinea-pig subcutaneously or intra-abdominally there are three distinct stages in the symptoms developed. The first is one of peripheral irritation characterized by restlessness and itching. The animal

scratches itself quite violently, not especially the point where the injection was made, but every part that can be reached with the foot. During the second stage the animal lies on its side or abdomen, quite limp; there is partial paralysis, most marked in the posterior extremities. The last or convulsive stage is characterized by more or less violent clonic convulsions, due to, and quite characteristic of, failure of respiration. The heart usually continues to beat quite regularly for some minutes after respiration has ceased. When the dose is administered intra-abdominally the quantity required to kill is reduced one-half and the symptoms follow one another more rapidly. In intravenous injection death occurs so quickly that a detailed study of the symptoms is quite impossible. Evidently the poison destroys life by its effect upon the cells of the respiratory centre. When introduced subcutaneously some of it is fixed apparently by the local cells, and the rest of it is slower in reaching the brain. Besredka<sup>2</sup> has found that ether narcosis prevents the fatal action of a second dose of horse-serum in animals sensitized to this fluid, and we find that the same means may save the life of an animal treated with a more than lethal dose of the free poison. A guinea-pig was given intra-abdominally 150 mg. (two and one-half times the lethal dose) of the free poison, and immediately thereafter was deeply narcotized with ether and held in this state for twenty minutes, and then allowed to recover. This animal showed no symptoms of the poison, while of two controls that received the same dose of the poison one died within five, and the other within seven minutes. It seems that the ether prevents the combination of the poison with the cells of the respiratory centre, and that the poison in the mean time is fixed by other cells, the continued function of which is not so directly essential to the continuance of life.

We have made numerous attempts with goats, rabbits, and guinea-pigs to produce an antibody to this poison, but have met with only negative results, and I have concluded that there is no antibody to this poison. Certainly there can be obtained from the animals with which we have worked nothing comparable to the antitoxin of diphtheria.

We have attempted to immunize animals against the living typhoid bacillus by repeated treatments with non-fatal doses of the free poison, and to a very mild degree we have succeeded in this. By proceeding carefully and gradually increasing the doses a point may be reached where the animal bears from two to three times the amount that would surely kill an untreated animal. Animals brought into this condition, whether it be one of increased tolerance or immunity, bear from two to four times the fatal quantity of the living bacillus. However, this tolerance is not specific; it can be induced quite as well with the poison obtained from egg-white, and

<sup>2</sup> *Annales de l'Institut Pasteur*, December, 1907.



it protects quite as well against the colon as it does against the typhoid bacillus, and, in my opinion, it is nothing more than increased tolerance for the poison that is common to all true proteid bodies.

I will now turn to the non-poisonous split product of the typhoid bacillus. This is the specific part of the cell; it is the antigen or the haptophor, and in it lies, in my opinion, the most promising hope for the specific treatment of typhoid fever. I have called this portion the "residue," as the part left after the extraction of the poison. The residue makes up about two-thirds of the weight of the cell substance; however, just as the poison consists largely of inert matter, so does the residue contain much that has no immunizing properties. As obtained by splitting up the cellular substance with the alcoholic solution of sodium hydroxide, the residue contains too much alkali to be injected into animals. It is, therefore, placed in Soxhlet's apparatus, extracted for some days with alcohol, then dried and powdered. To prepare a solution for use, this powder is weighed, shaken with 0.5 per cent. carbolic acid, and filtered through porcelain. Solutions thus made apparently retain their immunizing properties indefinitely. At least we have made some preparations that we have used for three years, and they are quite as efficient now as they were when freshly made. The residue, unlike the poison, is strictly specific. That from egg-white sensitizes the animal, after the proper period of incubation, to egg-white and to no other proteid, and that from the typhoid bacillus immunizes to this micro-organism and to no other. The residue does not sensitize to itself, with the exception of the residue obtained from the tubercle bacillus, which does sensitize to itself in guinea-pigs and in man. While it is not my purpose to enter into the detail of our studies of the tubercle bacillus in this paper, I will say that the tubercle proteid seems quite different from any other proteid, bacterial, animal, or vegetable, that we have studied. I have given this residue ordinarily in 10 mg. doses once a week to a patient for more than a year, with apparent benefit and certainly without any recognizable harm, and in other patients I have used a dose of 500 mg. without apparent injury, but even when the smaller dose of 10 mg. is not exceeded, if the interval between doses be six weeks or longer, the first injection after the long interval has, in two instances in the same patient, not in others, been followed by the well-marked and alarming symptoms characteristic of the so-called serum disease. I intend to give details with regard to the tubercle residue at some future time.

We have not gotten an active residue from all proteids. That obtained from casein does not sensitize to casein. This is not strange, since casein is known to differ from most other proteids in its molecular structure. It is possible that some other method of cleavage may give us a sensitizing residue from casein.

Wheeler and I<sup>4</sup> have proposed a theory of the action of proteid

<sup>4</sup> Jour. Infect. Dis., May, 1907.

residue which I will briefly summarize here, but before doing this it will be well to state as concisely as possible what we have found some of these residues to do. V. C. Vaughan, Jr.,<sup>5</sup> and Wheeler and I<sup>6</sup> have reported on the production of immunity to the colon and typhoid bacilli with their respective residues. In doing this work we have found it convenient to designate the minimum fatal dose of a twenty-four-hour beef-tea culture of the living bacillus as a unit in the measurement of the degree of immunity secured.

A single intraperitoneal injection of from 10 to 50 mg. of the typhoid residue protects a guinea-pig against at least twice the minimum fatal dose of a living culture of the typhoid bacillus given any time between the end of the first and of the fifteenth day after treatment with the residue. Frequent treatments with 10 to 50 mg. of the residue at intervals of two or three days give a more marked and a more lasting immunity against the living bacillus. With from six to nine such treatments the animal will bear from eight to ten times the minimum fatal dose of the living organism. If a small dose of the residue, not more than 12.5 mg., be given a guinea-pig intra-abdominally, and a minimum fatal dose of the living germ be injected within thirty minutes, the animal does not die, but if 50 mg. of the residue be given, and this be followed within thirty minutes by the minimum fatal dose of the living culture the animal will die, and indeed it may die from a smaller dose than that necessary to kill a control. To give the exact figures, we have found that 12.5 mg. of the typhoid residue protects a guinea-pig against six units of the living culture administered thirty minutes later, while 100 mg. of the residue so increases the susceptibility of the animal than even less than a single unit kills it.

The residue from egg-white, as has been shown by Wheeler and myself<sup>7</sup> and the residue from the proteids of the serum of the horse, as shown by Nicolle and Abt,<sup>8</sup> sensitize animals to their respective unbroken proteids. If the residue of egg-white be injected into a guinea-pig and ten days or more later this animal be treated with unbroken egg-white, it will be found that the animal is sensitized, it is made sick, and if the dose of egg-white is sufficient, it is killed. On the other hand, if the residue of the typhoid bacillus be injected into a guinea-pig, and later the animal be inoculated with six times the minimum fatal dose of a living typhoid bacillus, the animal will not die. The residue of egg-white or that of serum albumin sensitizes animals, while the residue of the typhoid or that of the colon bacillus immunizes animals. The sensitized animal dies from the second treatment, the immunized animal is protected. These conditions are apparently antipodal, and yet I hold that they are identical in essence. The residue of egg-white or serum albumin

<sup>5</sup> Jour. Med. Research, 1905, xiv, 67.

<sup>6</sup> New York Med. Jour., June 22, 1907.

<sup>7</sup> Jour. Infec. Dis., June, 1907.

<sup>8</sup> Annales de l'Institut Pasteur, February, 1908.

sensitizes the animal by developing in it a specific proteolytic ferment which is stored up in certain cells in the animal body as a zymogen; when, subsequently, unbroken egg-white or serum albumin is injected into the animal, this stored up zymogen is activated and the injected proteid is broken up so rapidly and its poisonous part is set free so abundantly that it combines with certain receptors in the cells of the respiratory centre, and kills the animal. Likewise the residue of the typhoid bacillus sensitizes the animal by developing a specific, proteolytic ferment, which is stored up in certain cells in the animal body as a zymogen; when, subsequently, the living typhoid bacilli are injected into this animal, the zymogen is activated and splits up the bacilli before they have time to multiply and produce a fatal dose of the specific poison. Egg-white does not kill the animal sensitized by its residue unless the amount given is sufficient to supply a fatal dose when it is split up. On the other hand, when the living typhoid bacillus is injected into an animal sensitized by its residue it will quickly kill it if it be injected in sufficient amount to supply a fatal dose of the poison when it is split up. In usual parlance, when we say that one loop or 1 c.c. of a given strain of the typhoid bacillus is fatal to guinea-pigs, we mean that animals inoculated with this amount die, but we do not mean that this amount kills them; it is what this amount develops into, during the ten or more hours of inoculation, that kills. Now, the difference between sensitizing an animal to egg-white with its residue and immunizing an animal to the typhoid proteid with its residue is wholly apparent and not real. In essence they are not two things, but one. The apparent difference arises from the fact that in one instance we are dealing with a dead, stable proteid, and in the other with a living, labile proteid. In both instances we are dealing with proteid susceptibility and sensitization.

When a proteid is split up in the body of an animal sensitized to it, it yields the same poison that we have obtained by cleavage of the proteid with alkali in alcohol. The animal that dies from the toxophor group split off chemically from egg-white and the one that dies from the injection of egg-white after sensitization die from the effects of the same poison just as truly as the man who dies from morphine and the one that dies from opium die from the same poison. In both the poison comes from the egg-white. The symptoms are identical in every particular; they originate in the same time, proceed in like order, and terminate alike; the mode of death is the same and the postmortem findings are identical. I must conclude that the process of sensitizing an animal to a proteid consists in developing in its body a substance or a ferment which splits up that special proteid just as the alcoholic solution of alkali does in the retort, but much more promptly and efficiently. That the proteid is split up in the animal body so as to furnish the same poison that is obtained in the retort there seems no opportunity for

reasonable doubt. Whether the sensitizing or immunizing residue results from the cleavage that occurs in the animal body is a question for the affirmation of which we have the following evidence: (1) If several guinea-pigs be killed by intraperitoneal inoculation with the typhoid bacillus, and the exudate that forms be removed and be freed from cellular elements by filtration through porcelain, this filtrate acts exactly like a solution of the residue as we have prepared it *in vitro*. Large doses of this filtrate given simultaneously with an inoculation of the living bacillus apparently increase the susceptibility of the animal, while a small dose increases the resistance of the animal to an inoculation made later, and repeated doses of the filtrate given at intervals of from two to three days give to the animal a marked immunity to the living bacillus, and this immunity is specific as is that obtained by our residue. The identity of this split product obtained by the cleavage of the bacterial cell in the animal body with the aggressin of Bail seems to me quite evident, or at least highly probable. (2) As was first shown by Gay and Southard,<sup>9</sup> the blood serum of an animal sensitized to the blood serum of another animal contains a sensitizing body, as may be shown by treating a fresh animal with it, and Nicolle and Abt<sup>10</sup> have shown that the residue obtained by splitting up the proteids of blood serum by our method sensitizes animals to the unbroken blood serum. Wheeler and Vaughan<sup>11</sup> have shown that the peritoneal washings from sensitized animals, dead from second injections, sensitize fresh animals.

From these findings I conclude that in the animal body the typhoid or colon proteid or egg-white, or serum albumin or serum globulin, or, in short, any true proteid is split up into residue and poison, much the same as it is in the retort by our method, but much more completely and perfectly. While the poison that kills in typhoid fever is the same in essence with that which we obtain from the typhoid proteid, the residue that sensitizes is also the same, whether it be obtained by chemical cleavage *in vitro*, or by the more perfect chemical cleavage *in vivo*. In one instance the active agent is the hydrolytic effect of dilute alkali; in the other it is a specific, proteolytic enzyme.

I will now attempt to apply this knowledge that we have obtained in the study of the chemistry of the typhoid bacillus, and the method of securing immunity to it to the disease of which it is the cause. In making this attempt I wish to state that what I may say is tentative and subject to modification from a wider and more exact knowledge that may come from more extended research. I do not say that an antibody to the typhoid poison will never be secured, but I do say that such a discovery is not probable. The fact that the fatal

<sup>9</sup> Jour. Med. Research, 1907, ii, 143.

<sup>10</sup> Annales de l'Institut Pasteur, February, 1908.

<sup>11</sup> Jour. Infect. Dis., June, 1907.

effect of the poison may be prevented by ether anesthesia is encouraging, and it is within the range of possibility that some more practical and usable agent to accomplish the same purpose may be secured.

When one becomes infected with the typhoid bacillus there is a period of incubation which, according to our best information, lasts some ten days or longer. In the guinea-pig inoculated with a fatal dose of the typhoid bacillus, the period of incubation continues for ten or more hours. During this period in both the man and the animal the bacillus multiplies, and yet there is no evidence that either the man or the guinea-pig is for the time being aware of the abnormal condition, or conscious of the presence of the undesirable guest. The sickness begins when the animal body becomes sensitized and begins to split up the bacilli. It is probable that this sensitization does not occur until some of the bacilli undergoing autolysis or being broken up by phagocytic action furnish the soluble residue which can reach a large portion of the body cells. We know that an individual may carry the typhoid bacillus in his gall-bladder or urinary bladder or in an abscess for years without having typhoid fever. The bacillus grows and multiplies in one of these cavities, and in greater or less numbers breaks up. The poisonous portion, being diffusible, is taken into the circulation and causes more or less marked departure from health, but the residue being non-diffusible, there is no general sensitization of the body.

Proteid sensitization may be local or general. There are certain reasons for believing that the sensitizer must reach a body cell before it can sensitize it. This is the reason why the residue fails to sensitize so long as it is confined to a cavity, such as the gall-bladder, and it also explains why the soluble residue produces general sensitization while the unbroken bacillus acts only locally and imperfectly. Moreover, this explains the development of acute poisoning with such soluble proteids as egg-white, blood serum, milk, etc. It is impossible to induce such explosive reaction with non-soluble proteids such as living or dead bacilli. When the first or sensitizing dose of a soluble proteid is administered every cell in the blood and lining of the bloodvessels is reached, and again, when the second or poisonous dose is administered the same cells are reached practically at the same moment, and according to our theory the zymogen in all these cells is activated at the same time, and the effect is explosive—an effect that can be produced only by soluble bodies. Again, when the poison is set free slowly much of it is probably fixed by the immediately surrounding tissue and the disastrous effect on the life of the animal that comes from an overwhelming action on the respiratory centre is avoided.

The fact that the administration of a large dose of the residue simultaneously with or very near in point of time with the inoculation with the bacillus increases the susceptibility of the animal,

while a much smaller dose of the residue increases the resistance, and repeated doses give immunity is an interesting fact. I have interpreted this finding as follows: The residue converts the zymogen into an active ferment, and, at the same time absorbs it. The attraction is between the residue and the ferment. The latter combines with the former more readily when it is free than it does when the residue is still a part of the bacterial cell. When large quantities of the residue are given the activated ferment is all or largely taken up by the free residue, and there is no splitting up of the bacterial proteid; consequently, the bacillus multiplies without hindrance; but when the zymogen is activated by only a small amount of residue, the greater part of the ferment is used in splitting up the bacilli. This is, I think, an important point, and in using the residue in the treatment of typhoid fever must always be borne in mind, because it must determine the dose of residue to be administered.

If the residue acts upon man as it does upon guinea-pigs, it should prove an efficient, but a temporary, vaccine against typhoid fever. In guinea-pigs a single injection of the residue gives the animal protection against twice the fatal dose of the living bacillus for about forty days, and it is presumable that it would protect against natural infection in which the number of bacilli introduced is much smaller for a longer time. That Wright's vaccination against typhoid fever was of some service in the Boer campaign seems quite well substantiated, but he employed the unbroken bacillus, while in animals at least the residue is much more efficient, because, as I have attempted to explain, the soluble residue gives a more general and consequently a more efficient sensitization than the unbroken bacillus, since the latter has to be split up before it can give any general sensitization at all. Besides, the residue causes no local irritation or inflammation about the point of injection, and the sensitization produced by it is systemic from the start. However, the possible use of the residue as a vaccine is not the special purpose of this paper, and the subject will not be farther pursued at present.

If my interpretation of our experimental work be correct, whether one treats typhoid fever with the residue obtained by splitting up the bacillus chemically or with the blood serum of an animal that has been treated repeatedly with the unbroken typhoid bacillus, in either case he uses the residue. In one case the residue has been obtained by chemical cleavage of the typhoid proteid *in vitro*, and in the other the residue has been obtained by ferment cleavage *in vivo*. An animal may be sensitized to egg-white by the residue obtained chemically as shown by Wheeler and I, or with the blood serum of a sensitized animal, as shown by Gay and Southard; or, an animal may be immunized with the residue of the typhoid bacillus obtained chemically, or by the filtered peritoneal exudate of an animal killed with the living typhoid bacillus. It is the residue in either instance that sensitizes or immunizes. If this be true there is every advantage

in favor of the employment of the residue obtained chemically. First, it is much less expensive to obtain the residue by chemical cleavage than by administration of the bacillus to animals; second, the residue makes a much better preparation, it is less bulky, and does not contain all the foreign matter that is contained in blood serum; third, in employing blood serum one risks sensitizing his patient to the proteids of blood serum while the residue does not sensitize to itself; and fourth, the dosage may be determined accurately with the residue obtained chemically.

If typhoid fever could be recognized in its early stages when sensitization and cleavage of the bacillus is only local and imperfect, then I should hope for great advantage in its treatment with the residue. This soluble sensitizing agent acting promptly as it does, might be expected to split up the bacilli before they become so numerous, and the abortion of the disease might be easily brought about. Reed, Shakespeare, and I<sup>12</sup> ascertained that many of the light febrile attacks among the soldiers in our camps in 1898 were typhoidal; they gave at least temporary immunity to the disease, and they responded to the Widal test. These abortive attacks are best explained on the ground of early systemic sensitization and destruction of the bacillus. Furthermore, we found that in its early stages typhoid fever is often apparently intermittent, and this is best explained as due to local and incomplete sensitization. If the disease could be generally recognized in this stage the residue should be of great service in aborting the disease. In this stage small doses of the residue, not more than 50 mg. should prove of marked service. It is to be hoped that some means for the early and positive diagnosis of this disease will soon be discovered.

The problem is quite a different one when it comes to the treatment of well developed typhoid fever, when there is an abundant bacteremia. In this stage one of the dangers to life is the too rapid and abrupt cleavage of the bacilli with the liberation of the poisonous group in such quantity that it may overwhelm the nervous system. Even here, however, the residue may be of service in the saving of life if wisely used, but it may prove a two-edged sword and cut both ways if not used with intelligence. Larger doses of the residue by absorbing or combining with the specific proteolytic ferment may retard the cleavage of the bacillus, diminish the quantity of poison set free in a certain time, and save the life of the patient, but with the effect of prolonging the disease as Richardson<sup>13</sup> has shown.

Richardson has shown the apparent value of the residue in preventing relapses in typhoid fever. The employment of the residue for this purpose seems to me rational and in accord with the general statements that I have made. In this disease there are often espe-

<sup>12</sup> Report on the Origin and Spread of Typhoid Fever in U. S. Military Camps during the Spanish War of 1898.

<sup>13</sup> Boston Med. and Surg. Jour., 1907.

cially resistant bacteria that escape the general lytic cleavage that destroys most of their fellows. These withdraw into the tissues, multiply, and then venture again into the circulation. Richardson's work apparently shows that a judicious stimulation of the function of sensitization serves a valuable purpose in preventing these relapses.

In conclusion I wish to say that, so far as I can see today, it is not probable that we will ever get an antitoxin for the treatment of typhoid fever comparable with that which we have for diphtheria, but that the residue may be of service, especially in preventing relapses, and if we can find some method of early diagnosis it may prove of value in aborting the disease.

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### **OBSERVATIONS ON THE HYPODERMIC USE OF QUININE AND UREA HYDROCHLORIDE IN THE DIAGNOSIS AND TREATMENT OF ACUTE AND CHRONIC MALARIAL INFECTIONS,**

AND ON THE RESEMBLANCE TO THE SEXUAL CYCLE OF THE HEM-  
AMOEBA MANIFESTED BY THE PERIODS OF FREEDOM FROM  
PAROXYSMS THAT ORDINARILY FOLLOW A SINGLE IN-  
JECTION OF ABOUT ONE GRAM OF THIS SALT.<sup>1</sup>

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THE object of this paper is to recall attention to four points in connection with the hypodermic use of quinine and urea hydrochloride in acute and chronic malarial infections: (1) The superiority of this salt over other preparations of quinine. (2) The periods of either six and one-half days approximately, or thirteen days approximately, during which patients previously exhibiting irregular recurrences of paroxysms, or regular quotidian, tertian, or quartan recurrences, remain free from paroxysms following a single injection of about 1 gram (15 grains) of this salt. (3) The similarity between these periods of six and one-half and thirteen days respectively, and the periods of cyst formation and of sporozoite development in the sexual cycle of the parasite, as observed in the mosquito. (4) The diagnostic value of such injections, both in proving and in disproving malarial infection in cases in which parasites have not been discovered in the peripheral blood.

<sup>1</sup> Read by title at the fifth annual meeting of the American Society of Tropical Medicine, Baltimore, March 28, 1908.



A fifth point may be emphasized in passing, as a variant of the first, namely, the probable therapeutic superiority of this quinine salt in pernicious malaria.

In connection with the similarity between the significant periods of the sporogony of the hemamceba and the week and two-weeks freedom periods following the use of quinine in this active form, I have sought, and had search made, for gametes and sporozoites, but without success. I am extremely desirous that the observations should be repeated by observers more skilled in technique and in parasitology, than I and having more continuous control of abundant material.

My experience with the use of the double hydrochloride of quinine and urea in the treatment of malarial infections dates from 1884, when I was chief of clinic in the Medical Out-patient Department of the Jefferson Medical College Hospital, in the service of Professor Roberts Bartholow, whose praise of this preparation led me to its use. Its advantage is extreme solubility, as it dissolves in its own weight of water, thus making possible the administration of a sufficient dose, which is quickly absorbed. Its disadvantage is the liability to produce slough or abscess if one is not careful in the use of the preparation. With due care to make the injection deeply under the skin, but not necessarily into the muscle, and to empty the syringe before withdrawing the needle, so that no drop of the solution shall fall upon the integument as the needle leaves the tissues, such accident need not be feared. An additional precaution invariably employed in my service is to seal the point of puncture with iodoform collodion or with tincture of iodine.

In G. E. de Schweinitz's experiments<sup>2</sup> upon quinine amblyopia, he found the quinine and urea salt much more toxic than any of the other preparations which he employed. Incidentally to the therapeutic studies summarized in the following pages, observations have from time to time been made as to the effect of the drug upon leukocytosis. So far as the gross leukocyte count is concerned, it frequently seemed to reduce the number slightly, but this effect was not invariable, nor did the decrease persist for more than forty-eight hours after the injection. Not rarely, the fall would be followed by an increase above the previous figure. As to differential counts, the observations are insufficient and inconclusive.

**ACUTE MALARIAL INFECTION.**—The observations which here are summarized have been carried out in private practice, at the Jefferson Medical College Hospital, both in the Out-patient Dispensary and in the wards, and at the Philadelphia Hospital. Unfortunately, some of the records have been mislaid, so that accurate statistics cannot be given. Approximately, there have been treated by this

<sup>2</sup> Personal communication; also G. E. de Schweinitz, *Toxic Amblyopias*, Philadelphia, 1896, p. 193

method about 250 cases of acute malarial infection, of which 1 was of quartan periodicity, upward of 100 of quotidian periodicity, and upward of 140 of tertian periodicity, the remaining 5 or 6 exhibiting irregular recurrence. In the 1 case recorded as of quartan periodicity the parasite was identified as the quartan parasite (*Hæmamoeba malaris*). In the others the tertian parasite, of the ordinary (*Hæmamoeba vivax*) or estivo-autumnal (*Hæmamoeba falciparum*) type was, in general, recognized. Unfortunately, the records, while noting the presence or absence of organisms, fail to specify in a sufficient number of cases the exact variety found. It is possible that in some cases quotidian parasites were present and not identified.

In all cases of which note was made, with the exception of 4 instances in which two injections were necessary to bring about the freedom period, there occurred, following a single injection of 1 gram of the quinine and urea salt, especially if this were administered during the paroxysm or within four hours thereafter, a prolonged, definite period of freedom from paroxysms. In about one-third of the cases this lasted between six and seven days, varying from one hundred and forty-one to one hundred and sixty-two hours; in the remaining two-thirds of the cases, the period of freedom was between twelve and fourteen days, varying from two hundred and ninety to three hundred and twenty-five hours. In some of the case-notes these periods are estimated from the beginning of chill to the beginning of chill, and in some cases from the hour of maximum temperature to the hour of maximum temperature. In future observations a uniform method should be followed. It is also quite possible that nurses on duty do not always catch the exact beginning of a chill, or the exact point of maximum temperature. I am inclined to believe that a fair statement of the average freedom periods would be six and one-half and thirteen days respectively; or perhaps it might be stated as seven and fourteen (week and fortnight) *organism days* of about twenty-one to twenty-two hours each. The most frequent figures to be found in the notes concerning the week-cycle are one hundred and forty-seven, one hundred and fifty, and one hundred and fifty-six hours; in the notes concerning the fortnight cycle, three hundred, three hundred and six, and three hundred and twelve hours. As a rule, but not invariably, the cases showing the shorter period of freedom were quotidian in type. Of those exhibiting the larger period, the preponderating number were tertian. The quartan case showed a freedom period of twelve and three-eighths days, with certain peculiarities, a summary of which is given later.

When the injection is made within less than two hours before the time of an expected paroxysm, it usually does not prevent the occurrence of the chill, although the phenomena are, in general, milder than usual. The paroxysm due to follow will, however,

be missed, and the freedom period thereafter be manifested. When the injection is given three or four hours before the time at which a paroxysm is anticipated, it usually prevents the attack. When given between four and eight hours in advance of the expected chill time, the injection will usually prevent both the paroxysm about to be due and its anticipated successor, but sometimes only the latter. The effect cannot be predicted with certainty.

Usually the paroxysms, if tertian, would, after the thirteenth day, resume their former periodicity; or, if quotidian, would, after six and one-half or thirteen days, change to tertian. Rarely did the paroxysms resume the quotidian periodicity. A case of irregular periodicity would assume the tertian, less frequently the quotidian, type. In one instance there is a note made that the paroxysms changed from quotidian to quartan, but as the detailed records are missing and the case dates back to 1885, at which time the specific quartan parasite would not have been recognized, no stress is laid upon this fact.

In other cases, of which 6 are noted (probably all that were observed), after the six and one-half days or thirteen days of freedom, a further freedom period of six and one-half or thirteen days was manifested without further medication; that is to say, the periodicity apparently changed from quotidian or tertian, as the case might be, to what were formerly termed, respectively, the weekly and the fortnightly types. The number of possible observations of this kind was limited, for obvious reasons.

After the occurrence of the freedom period had been demonstrated, and the periodicity of the renewed paroxysms determined, injections were, as a rule, resumed and continued daily in quotidian cases, and on alternate days in tertian cases, until the recovery of the patient was assured; or the drug was administered by the mouth—in capsule—in two doses of 10 or 12 grains (0.75 gram) each, four hours and eight hours, respectively, before the anticipated chill time; or 10 grains (0.65 gram) were given at night and the same quantity in the morning, without special reference to the chill period; or one dose of 20 to 23 grains (1.3 to 1.5 grams) was given between eight hours and four hours before the anticipated chill. On the whole, one method answered as well as another.

When two weeks had passed without paroxysms, the patient was usually dismissed from the hospital, with the injunction to take 20 grains of the drug weekly, in two doses, one of 10 grains on the evening of the sixth day, and one of 10 grains on the morning of the seventh day, calculating from the date of the last paroxysm; and to continue this treatment for at least three months, returning to the hospital or reporting to the Out-patient Department from time to time, for observation.

The case of H. J., observed in October and November of 1907, may be related as a typical instance, illustrating several of the phenomena summarily described (Chart I).

This man had a quotidian intermittent fever, with paroxysms recurring in alternate periods of twenty-one and twenty-four hours. He exhibited the ordinary tertian parasite, and was evidently infected with two broods, maturing at forty-five hours. An injection was given fifty minutes before a paroxysm expected at 11 A.M., on October 26. The chill occurred on time, but its duration was much shortened. The temperature, which in previous attacks had risen to 104° or 105° F., reached only 103°, and fell to the minimum point, 97°, five hours after its maximum had been reached, the fall in previous paroxysms having occupied eight hours. There was no chill on the following day, and the temperature remained practically normal, oscillating between 97° and 98.4° until one hundred and forty-seven hours after the chill, or one hundred and forty-two hours after the temperature had fallen to its minimum. On November 1, the sixth day after the last preceding paroxysm, or the seventh day, including the day of that paroxysm, the temperature rose at 2 P.M. to 102°, remaining elevated for three hours, and reaching normal at 8 P.M., but there was no chill; the paroxysm was incomplete. On November 3, at 9.45 A.M., about forty-three and one-half hours after this incomplete paroxysm, a chill began, and the maximum temperature point of this attack, 104°, was reached at 11 A.M.; that is, about forty-five hours after the maximum point of the paroxysm without chill that had preceded it. The temperature reached its minimum at 8 P.M. A chill occurred at 7.15 A.M. on the fifth of November, again about forty-five and one-half hours after the previous chill, maximum temperature being reached at 8.45 A.M., and minimum temperature not until 2 A.M. the following day. The next chill occurred on the 7th of November at 7.45 A.M., forty-eight and one-half hours after the previous one, maximum temperature occurring at 11 A.M. and minimum temperature at 11 P.M. The fall of temperature was possibly hastened by the second injection of quinine and urea hydrochloride, which was given during the declining stage of this paroxysm, at 2 P.M. No further paroxysm was permitted to occur. The treatment was continued by injections on alternate days until November 16, and the patient left the hospital, apparently well, on November 18.

Examination of the blood had shown the presence of parasites in various stages; hyaline, pre-segmenting, segmenting, intracellular pigmented, and extracellular pigmented forms being present, all in large numbers.

October 24. 200 fields were counted and 600 parasites found.

October 25. A similar count was made.

October 26. 200 fields were counted; 560 parasites were found.

On this day an injection was given.

October 27. 200 fields were examined; 12 parasites were found—8 intracellular pigmented and 4 extracellular.

October 29. 200 fields were examined; 3 parasites were found—2 intracellular pigmented and 1 extracellular.

October 30. 500 fields were examined; no organisms were found.

October 31. 500 fields were examined; no organisms were found.

November 1 (the sixth day after the injection). 200 fields were examined; 34 parasites were found—young hyaline, 31; mature intracellular, 2; extracellular pigmented, 1. It was on this date that the temperature reached  $102^{\circ}$  at 2 P.M.

November 2. 200 fields were examined; 90 parasites were found—hyalin, 8; intracellular pigmented, 60; pre-segmenting, 22; segmenting parasites were specially looked for, but none found.

November 3. 200 fields were examined; 49 parasites were found—hyaline, 22; intracellular pigmented, 10; pre-segmenting, 16; segmenting, 1. On this day the chill occurred, with a temperature of  $104^{\circ}$ .

November 4. 200 fields were examined; 288 parasites were found—hyaline, 20; intracellular pigmented, 264; segmenting, 4. Temperature was  $102^{\circ}$  at the time of observation, but no chill occurred.

November 5 (last chill day). 200 fields were examined; 236 parasites were found—hyaline, 188; intracellular pigmented, 32; segmenting, 16. Injection was given on this day. No further chill occurred, and the number of parasites steadily diminished until finally they disappeared.

The accompanying charts, for which I am indebted to Drs. Robinson and Moore, internes at the Philadelphia Hospital, exhibit the decrease, disappearance, and return of parasites in this case and the temperature curves indicative of periodicity and freedom preceding and following the injection of the drug (Charts I, II, III).

One other case—that of quartan fever, being the only example of its kind in the series—may be cited in brief summary. It shows a period of freedom of twelve days and nine hours, interrupted by abortive disturbances on the intermediate days of paroxysm, and an apparent tendency to alternate periodicities of seventy-eight and eighty-four hours respectively. Whether the twenty-one-hour and forty-two-hour disturbances noted may not have some relation with quotidian and tertian periodicities, and what are the possibilities of a multiple infection, or of changes of type in organisms, are questions suggested by the case, but not answered (Chart IV).

Cosmo di G., aged twenty-three years, a native of Italy, by occupation a laborer, came into the hospital on June 17, 1907, with a history of having had an attack of chills and fever in Italy four years earlier, the paroxysms, according to the patient's statement, recurring after intervals slightly in excess of three days. The duration of this attack was three weeks, and the patient, although he suffered from irregular fever on various occasions thereafter, had had no second attack. The present illness began about five weeks before admission to the hospital, with a violent chill, which lasted about three hours and was followed by fever and sweating. Later, severe muscular pains developed, with extreme tenderness, especially of the trunk and abdomen. This was followed by the appearance of

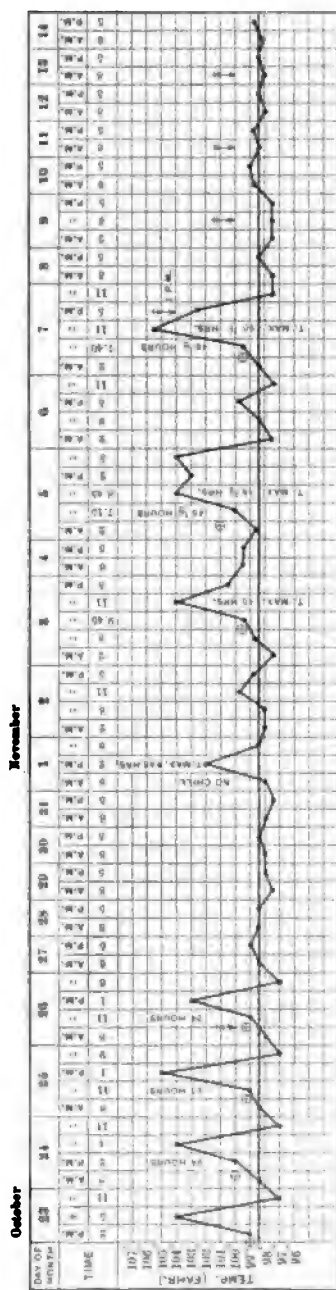


CHART I.—Quotidian intermittent fever. Free period 147 hours. Change of type to tertian. (Henry J.; Autumn, 1907.)

! Injection of 1 gram of quinine and urea hydrochloride.

• **Beginning of chill.**

what, from the patient's description, seems to have been a maculopapular eruption, lasting about one day. According to the patient's statement, these paroxysms recurred every third day, and were followed by a like eruption. He had been given some pills, presumably quinine sulphate, but had not recovered.

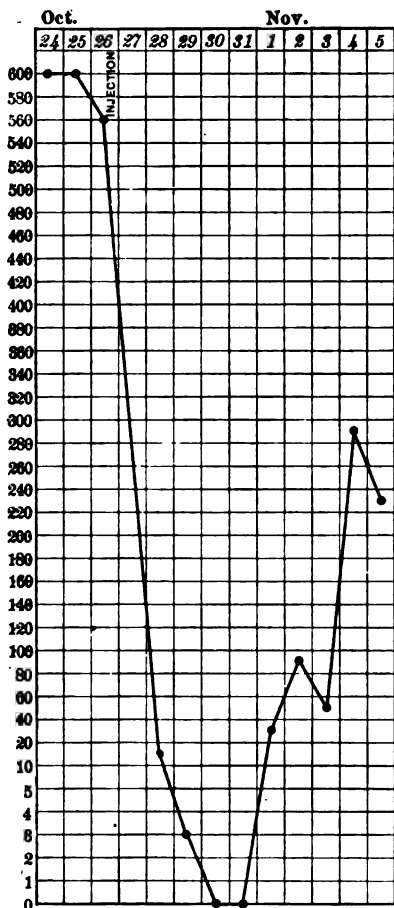


CHART II.—Showing disappearance and reappearance of organisms after the injection of 1 gram of quinine and urea hydrochloride. (Case of H. J.)

Physical examination of the patient upon admission revealed nothing significant, other than slight enlargement and tenderness of the spleen. Irregularly distributed over the trunk and abdomen was a papulo-œdematous eruption, consisting of central spots of a pinkish color, surrounded by a purplish areola. This gradually faded, reappearing with high temperature paroxysms. After treat-

ment was begun it disappeared altogether. The temperature upon admission was 101.3° at 5 P.M., June 17. Chart IV shows the course of the temperature during the patient's stay in the ward. Previous to the injection of 1 gram of quinine and urea hydrochloride, three periods of maximum temperature (about 103° F.) were noted, the intervals being, respectively, eighty-four hours and seventy-eight hours. Periods of minimum temperature (about 97° F.) followed the maximum temperature after intervals of, respectively, twenty-four, thirty-six, and twenty-four hours. Each of the periods

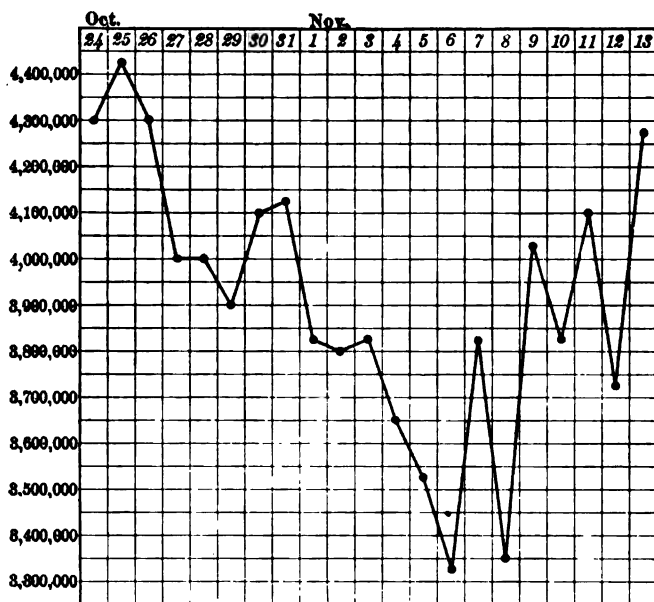


CHART III.—Erythrocyte count diminished after injection of quinine and urea hydrochloride (October 26), until disappearance of recrudescence organisms; then increasing interruptedly. The leukocytes varied during this period from 4800 to 4000, falling to the latter number on October 28, when the temperature became normal following the injection, and the parasites were only 12; they gradually rose, with remissions in count up to 4400 on November 5, when the temperature was 104.2°, and the number of parasites was 236. (Case of H. J.)

of maximum temperature was preceded by a chilly sensation and followed by sweating. The decline of temperature to the normal point, or just above, occurred in from three to twelve hours, without medication.

The blood on the day following admission showed: hemoglobin, 100 per cent.; erythrocytes, 5,104,000; leukocytes, 13,800—polymorphonuclear, 73 per cent.; small lymphocytes, 13 per cent.; large lymphocytes, 13 per cent.; eosinophiles, 1 per cent. No organisms were found in several slides prepared from the fresh blood, nor were



they discovered either in stained or unstained specimens until the 26th, when intracorpuscular forms were seen. On the 28th, the day on which the paroxysm, if quartan, was again due, both intra-

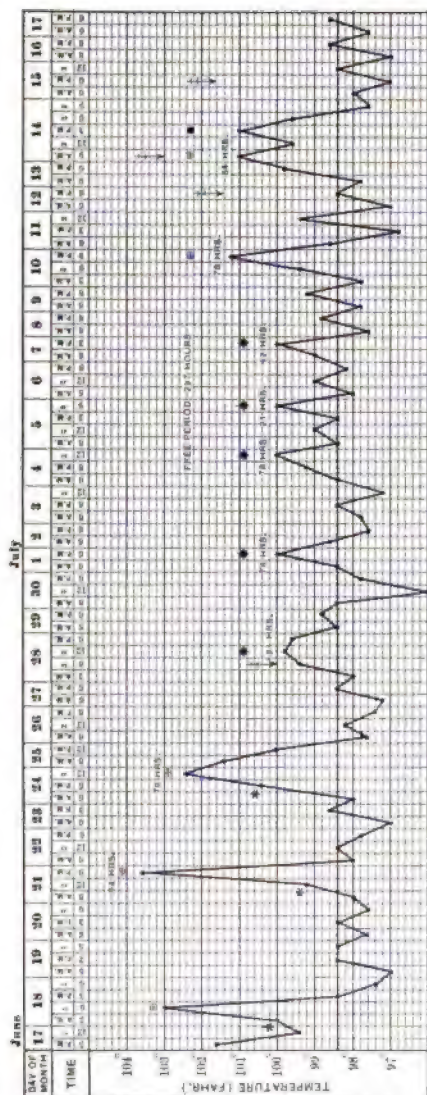


CHART IV.—Quartan intermittent fever. Free period 297 hours. (Cosmo di G.; Summer, 1907.)  
 \* Beginning of chill.  
 ♦ T. rise without chill.  
 † Injection of 1 gram of quinine and urea hydrochloride.  
 • End of chill.  
 ■ Double crest temperature rise.

corpuscular and extracorpuscular forms were identified as the quartan parasite.

On June 28, at 6 A.M., six hours in advance of the paroxysm anticipated on that day, which was apparently due to occur eighty-four

hours after the preceding paroxysm, the injection was given, the temperature at that time being 99.4°. No chilliness was felt, but the temperature rose 4 points to 99.8° F., about 3° less than the preceding maximum point and 4° less than the paroxysm with which its period of eighty-four hours apparently related it. No further injection being given, a period of temperature rise (100°) manifested seventy-eight hours later, another rise, again after seventy-eight hours, another twenty-one hours later, and another forty-two hours later. The patient complained of nothing. There was neither chilly sensation nor what might be considered marked rise of temperature until July 10, at 9 P.M., seventy-eight hours after the rise of temperature last noted, two hundred and ninety-seven hours (twelve days and nine hours) after the abortive temperature rise following the injection, and three hundred and eighty-one hours after the last preceding definite paroxysm. The next paroxysm, with a temperature rise to 101°, occurred July 14, at 9 A.M., the interval being eighty-four hours. This paroxysm shows a double crest, the second rise occurring six hours later than the first. Following this, injections were given at such intervals as to control the paroxysms and assure recovery from the acute attack. Treatment appropriate to chronic malarial infection was then instituted.

During the period of observation the following notes were made concerning organisms:

June 26. Malarial organisms found—intracorpuseular forms.

June 27. Malarial organisms found.

June 28. Organisms—quartan—found. Injection given.

June 29. Coarsely granular bodies—intracellular, peripherally located. A few hyaline bodies found.

June 30. Extracorpuseular and intracorpuseular bodies found. The intracellular bodies were oval in shape.

July 1. None found.

July 2. Intracellular bodies, with coarse pigment, sluggishly motile; extracellular pigmented bodies.

July 3. Same as above, pigment more peripheral.

July 4. Same as above.

July 5. Nothing found.

July 6. Nothing found.

July 7. Nothing found.

July 8. Motile bodies (intracellular) found.

July 9. Motile bodies (intracellular) found

July 10. Temperature rise. Intracorpuseular forms and extracellular motile bodies found.

July 11. Intracorpuseular forms and extracellular motile bodies found.

July 12. No parasites found.

July 13. Parasites found, pre-segmenting forms.

July 14. Paroxysm. Injection given. A few parasites.

July 15. None found.

July 18. None found.

July 30. None found.

Temperature charts are also shown of a number of cases taken at random (Charts V, VI, VII). It will be observed that in one of these quinine chlorhydrosulphate was used instead of the urea salt and was in this instance efficacious. Other observations were made with it. While therapeutically active, it did not prove so uniformly dependable as the urea salt in the matter of the defi-

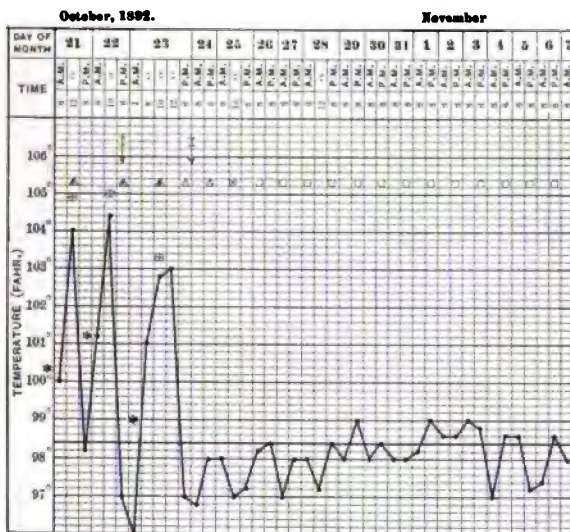


CHART V.—Quotidian intermittent of 30 days' duration prior to treatment. Two injections. Recovery. (John S.; Autumn, 1892.)

\* Beginning of chill.

+ End of chill.

† Injection of 1 gram quinine and urea hydrochloride.

▲ Organisms, pigmented, numerous.

△ Organisms, pigmented, few.

● Organisms, hyaline, few

○ No organisms.

nite freedom period. Drawings of parasites observed were made in 1892, by Dr. Claribel Cone, then interne at the Philadelphia Hospital and now professor of pathology in the Woman's Medical College of Baltimore, to whom I am also indebted for careful notes of the cases which were under her immediate care.

**CHRONIC MALARIAL INFECTIONS.**—In chronic malarial infections of long standing, especially in those cases which exhibit considerable enlargement of the spleen or liver, or both, with or without marked alterations of the blood, quinine alone, even in the form of the combination with urea, has not been sufficient to bring about recovery.

The quinine and urea salt, however, has seemed more efficacious than other preparations of cinchona and its alkaloids, with the exception of cinchonidine salicylate, and in no case has treatment without quinine been so satisfactory as when quinine has been used in con-

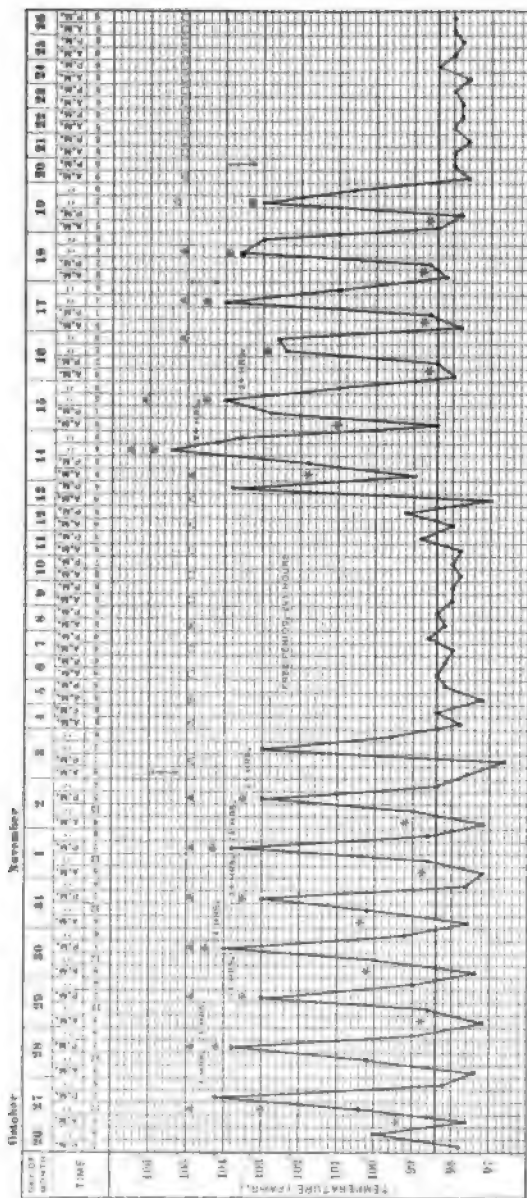


CHART VI.—Quotidian intermittent. Free period 291 hours. (Jos. D.: Autumn, 1892.)

\* Beginning of chill.

† Injection of quinine and urea hydrochloride.

△ Organisms, pigmented, few.      ○ No organisms

• End of chill.

▲ **Organisms, pigmented, numerous.**

2. **Organisms, hyaline, few.**

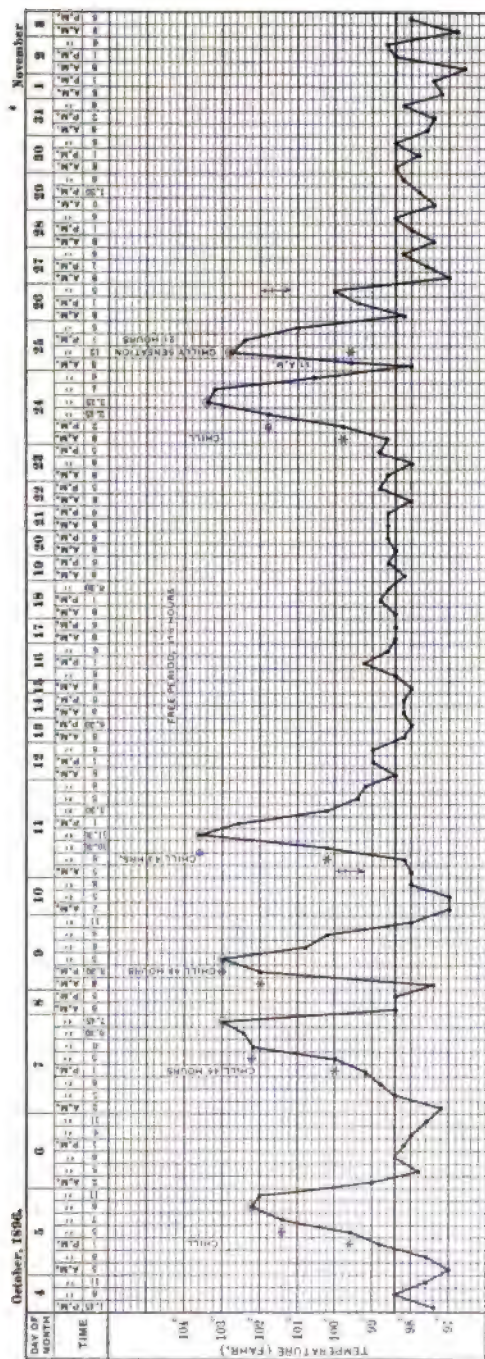


CHART VII.—Tertian intermittent. Free period 316 hours. (A. B. C.: Autumn, 1896.)  
 \* Beginning of chill.  
 † End of chill.  
 ‡ Injection of 1 gram of quinine chlorhydro sulphate.



junction, at various times, with salicin, methylthionin hydrochloride, arsenic, iodine, iron, and radiotherapy.

In those cases of chronic malaria in which there is a tendency to recurrence of acute exacerbations, whether manifesting as chills and fever or as gastric or nervous disturbances, the quinine and urea hydrochloride has been of distinct advantage in two ways: (1) When the recurrence is periodic, or assumes, after its initiation, a periodic type, quinine and urea hydrochloride used hypodermically or by the mouth, in appropriate dosage, and at a suitable time, will cause the acute symptoms to disappear promptly. For the remedy of the underlying cachexia or chronic affection, other means are additionally necessary.\* (2) In cases in which the symptoms are irregular the injection of a small dose of quinine and urea hydrochloride will frequently bring about some definite order, either in the quality or time of the symptoms; after which they can be dealt with in the same manner as cases spontaneously definite and periodic. In addition, the diagnosis is frequently made clear by the appearance in the peripheral blood of hemamœbæ, sometimes of atypical character, but still recognizable as varieties of the malarial parasite. This phenomenon will be spoken of more particularly in the next division of the subject, which concerns diagnosis.

DIAGNOSIS.—In two ways has the hypodermic use of the double hydrochloride of quinine and urea proved useful in diagnosis.

1. There are certain cases, evidently of acute infection, which resemble malarial fevers in the character or periodicity of the paroxysms, but in which malarial organisms cannot be found in the blood. There are certain other cases in which, despite the aberrant nature of the paroxysms, there is reason to suspect a malarial origin or complication, and in which, nevertheless, malarial hemamœbæ have not been discovered. In nearly every instance of either of these groups the presence or absence of malarial infection can be predicated upon the patient's reaction to a single injection of the urea and quinine salt. The prolonged freedom period having been found to occur invariably in every case in which the organisms had been demonstrated, it is reasonable to assume that its occurrence indicates the dependence of the symptoms upon undiscovered, perhaps deep-dwelling parasites, and that its absence means the absence of malarial infection.

Thus, in the course of the earlier observations at the Philadelphia Hospital, at a time when 5 cases of intermittent fever of definitely proved malarial origin were under treatment, and manifesting, some the six and one-half days, and others the thirteen days, freedom period, there was a sixth patient who exhibited what appeared to be a typical temperature curve of quotidian intermittent fever, but in

\* See also the author's articles in "The Polyclinic," Philadelphia, February 15, 1884, and January 15, 1886; and "The Philadelphia Polyclinic," March 15, 1893, and September 3, 1898.

whose blood malarial organisms could not be demonstrated. He received a diagnostic injection of 15 grains of quinine and urea hydrochloride, which induced merely a temporary fall of temperature. Renewed questioning then elicited from the patient what had theretofore been denied, namely, a history of syphilitic infection some six months previously; and recovery promptly followed the use of mercurial inunctions.

In cases of typhoid fever, in which the temperature has tended to assume, at some period of the case, an intermittent type, but in which malarial organisms have not been found in the peripheral blood, diagnostic injections have, in some instances, been followed by the freedom period and in others have not so been followed. In these

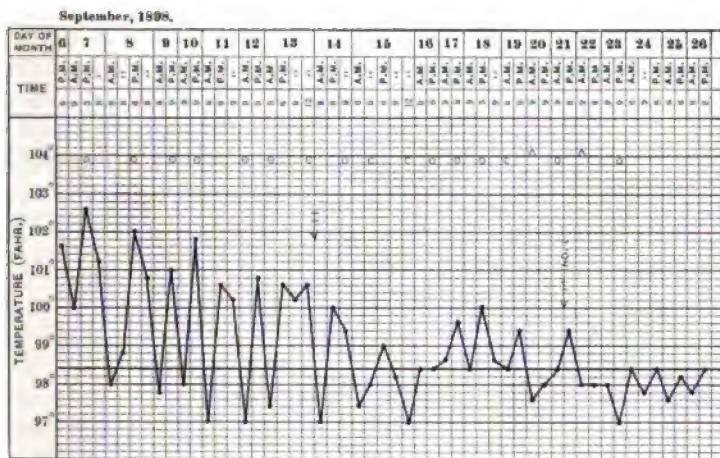


CHART VIII. (Illustrating diagnosis).—Mixed infection; typhoid and malaria. Widal reaction positive. Rose spots. (X. Y Z.; from Tampa, Fla.)

† Quinine and urea hydrochloride injected.      ○ No organisms found.  
 △ Organisms found.

instances, and especially among soldiers of the Cuban war, observed in the months of July, August, and September, 1898 (Chart VIII), it was found that the freedom period usually occurred in patients whose marked loss of hemoglobin would in any event have raised suspicion as to malarial complication, that is to say, of double infection—malaria and typhoid. In some of those in whom the quinine treatment was not continued, because it did not seem to be clinically necessary, the malarial organisms made their appearance during convalescence, after the typhoid infection had run its course. In others, the continuance of the quinine treatment presumably prevented such definite demonstration of the diagnosis. In those cases in which a single injection of the quinine and urea salt had a temporary antipyretic effect, but was not followed by a prolonged freedom

period, malarial organisms did not make their appearance so long as the patients remained under observation; and it is fair to conclude that in these cases that form of infection was absent.

2. The other method in which the injection of the quinine and urea salt has proved useful diagnostically has already been referred to in speaking of the treatment of chronic malarial infection. It was suggested to me by an old observation of Archibald Billings.<sup>4</sup> In cases of doubtful diagnosis the injection of a quantity of the drug not sufficient to secure a definite freedom period will frequently cause the appearance in the peripheral blood of organisms recognizable as normal or atypical forms of the hemamoeba of malaria, and this has been observed so frequently and in so many diverse conditions that I am inclined to look upon its absence after, say, half a dozen injections, varying from three days to a week apart, and in doses increasing from 0.3 to 1 gram, as virtually excluding malarial infection. A typical instance of the value of this use of the quinine and urea salt is the case of chronic malarial infection with splenomegaly and blood changes resembling those of Banti's disease,<sup>5</sup> studied in conjunction with Dr. R. C. Rosenberger and presented to the College of Physicians of Philadelphia, in March, 1904. I am of the opinion that in such cases the organism is resting in some larval form—if the expression be appropriate—probably in the spleen or bone marrow, and that its appearance peripherally is part of a defensive, reproductive reaction to the paratoxic effect of quinine. That organisms do remain latent for long periods is well known; and I have elsewhere referred to a case in which they had reappeared annually for twenty years, provoking, usually, a gastric crisis. This phase of the subject, also, I hope some competent investigator will look into.

<sup>4</sup> A. Billings, *First Principles of Medicine*, London, 1838, p. 218. <sup>4</sup>

<sup>5</sup> *AMER. JOUR. MED. SCI.*, August, 1904; *Trans. Coll. Phys. Phila.*, 1904; *Phila. Hosp. Reports*, 1905.



**THE RESISTANCE OF DIABETICS TO BACTERIAL INFECTION.**

A STUDY OF THE OPSONOPHAGOCYTIC PROPERTIES OF THE BLOOD IN  
74 CASES OF DIABETES MELLITUS AND RELATED CONDITIONS.<sup>1</sup>

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DIABETES mellitus, always an inviting field for research, appears to offer particularly attractive possibilities in connection with its bearing upon the opsonic properties of the blood, which, it seems reasonable to presume, should be more or less influenced by the pronounced metabolic disturbances incident to this disease. Especially is this true of cases attended by excessive glycosuria, and of those characterized by glaring inadequacy of fat oxidization, whereby the acetone bodies accumulate unduly in the blood and in the other tissues of the body, thus rendering the subject prone to the dangers of acid intoxication. The well-recognized susceptibility of the diabetic individual to boils and carbuncles, to spontaneous gangrene, and to pulmonary tuberculosis also argues, on a *priori* grounds, some deviation from the normal opsonin values, either as a cause or as a consequence of these complications. Furthermore, one is tempted to accept as more than an alluring theory a possible relation between the opsonic function and the hormone body "secretin," which substance, having been proved by Bayliss and Starling<sup>2</sup> to be an active factor of pancreatic secretion, was found to exist in minimal quantities in the non-pancreatic type of diabetes by Bainbridge and Beddard,<sup>3</sup> and more recently has been studied by Wentworth,<sup>4</sup> and by Sweet and Pemberton,<sup>5</sup> with relation to diabetes and other states of defective nutrition.

With the foregoing premises in mind, we have thought it worth while to investigate, in a reasonable number of diabetic subjects, the condition of the hemic resisting powers, as reflected by the behavior of the opsonic and phagocytic values in the individual instance. It is aside from the main question here to interpret the significance of opsonins and their effects upon the mechanism and other phases of

<sup>1</sup> Read at a meeting of the Section on General Medicine of the College of Physicians of Philadelphia, March 9, 1908.

<sup>2</sup> Jour. Amer. Med. Assoc., 1907, xlviii, 524.

<sup>3</sup> Jour. Amer. Med. Assoc., 1907, xlix, 204.

<sup>4</sup> Biochem. Jour., 1906, i, 429.

<sup>5</sup> Arch. Inter. Med., 1908, i, 231.

bacterial invasion, and for information about these fundamental details original sources should be consulted.<sup>6</sup> It is sufficient for the purposes here served to note that it is justifiable to regard opsonins as substances native to normal blood plasma which act upon various invading bacteria so as to render them easily phagocytized by the leukocytes; it is also probable that the erythrocytes are prepared for phagocytosis in an analagous manner, by the effect of the so-called "hemoposinin" of the blood; and a similar crippling of certain animal parasites—notably the trypanosome and the spirochete of relapsing fever—is believed to occur as an act preparatory to the engulfment of these microorganisms by phagocytes.

The present series of 52 cases is a supplement to the 22 reported by one of us (Da C.) a year ago, as a preliminary record of "The Opsonic Index in Diabetes Mellitus,"<sup>7</sup> which showed that in this disease the subject's opsonic powers are appreciably diminished, in comparison with those of a normal person, while in diabetes insipidus and in conditions of transient glycosuria no such deviation can be distinguished. The combined series of 74 cases, herewith reported, includes 50 examples of true diabetes mellitus, 4 of diabetes insipidus, 8 of non-diabetic glycosuria, and 12 of furunculosis and acne unattended by glycosuria. The data relating to this series is based upon 850 direct and control blood examinations, plus numerous repeated tests, bringing the total number of examinations close to the thousand mark. Most of the clinical material was supplied by the Jefferson, the German, and the Philadelphia General Hospitals, but for a number of referred patients we are indebted to several medical friends, especially to Dr. O. H. Petty, Dr. S. A. Munford, and Dr. J. H. Gibbon. The technical part of the work was done, through the courtesy of Prof. H. A. Hare, in his Laboratory of Clinical Medicine and Therapeutics at the Jefferson Medical College Hospital.

In the report just alluded to, it was shown that a diabetic's opsonic index to *Staphylococcus pyogenes* is subnormal; in this new group of 34 patients we have continued our studies with this bacterium, and, in addition, sought to determine the behavior of the blood opsonins in connection with two other varieties of bacteria, *Streptococcus pyogenes* and *Bacillus tuberculosis*. These microorganisms were selected as test-bacteria on the assumption that to such sources of infection the diabetic is peculiarly susceptible, and in this con-

<sup>6</sup> These contributions give the essential data and the literature of opsonins and the diagnostic and therapeutic application of the opsonic theory: Wright and Douglass, *Proc. Roy. Soc.*, 1903, lxi, 357; *Ibid.*, 1904, lxiii, 128, 135, 147; Wright, *Lancet*, 1907, ii, 423, 1213; Ross, *Brit. Med. Jour.*, 1906, ii, 1452; *Jour. Amer. Med. Assoc.*, 1907, xlix, 245; Crace-Calvert, *Lancet*, 1907, i, 279; French, *Brit. Med. Jour.*, 1907, i, 256, 882; Ehrlich, *Lancet*, 1907, i, 279; Simon and Lamar, *Johns Hopkins Hosp. Bull.*, 1906, xvii, 27; Hektoen and Reudiger, *Jour. Infect. Dis.*, 1905, ii, 128; Potter, Bradley, Ditman, and Bradley, *Jour. Amer. Med. Assoc.*, 1906, xlvii, 1722, 1793; Miller, *Ther. Gas.*, 1907, xxx, 173.

<sup>7</sup> *AMER. JOUR. MED. SCI.*, 1907, cxxxiv, 57.

nection it may be noted that in 56 per cent. (28 cases) of our diabetic patients complications traceable to these germs existed.

**TECHNIQUE.** The technique used in all our estimations was essentially that of Wright,<sup>8</sup> with certain modifications of minor importance suggested by our increasing familiarity with the work, bred of some eighteen months experience with it. But in addition to computing merely the opsonic index to the three types of bacteria mentioned, we have also determined, in each of the new patients, the number of phagocytes in a given number of leukocytes, as well as the number of bacteria adherent to, although not actually engulfed by, the leukocytes, irrespective of their phagocytic proclivities. Thus the opsonizing properties of the blood plasma are indexed by the first process, the proportion of potential phagocytes is calculated by the second, while the last procedure may have, we fancy, some more or less close relation to the one immediately preceding.

The method of calculating the ordinary opsonic index is now so well known that it is unnecessary to recount the details in this place. Those interested will find a description of our technique in an (Da C.) article in this Journal for July, 1907.<sup>9</sup> It may, however, be noted that, for the sake of uniformity, only polynuclear neutrophile leukocytes were counted as phagocytes, since this rôle is so infrequently and so indifferently assumed by large mononuclear leukocytes that, to all intents and purposes, they are a negligible quantity in opsonophagocytic estimates.<sup>10</sup>

The richness of the blood in phagocytes was studied by ascertaining their percentage in the patients' blood, and by comparing this value with a corresponding value for normal blood (considered as 1), thus obtaining a figure that may be expressed as the "phagocytic index." Under the term "percentage index" Simon has described in detail this method of research.<sup>11</sup>

Our object in taking account of the attached or attracted bacteria was to discover what bearing, if any, such a condition has on true phagocytosis. Having repeatedly observed specimens of blood containing few phagocytes, but many leukocytes with numerous bacteria tightly adherent to their peripheries, this question arose: Does such a picture mean actual crippling of the cells' phagocytic powers, whereby bacteria are apparently attracted, but not engulfed; or can it be explained simply by some coincidence, or by an error in technique, such as, for example, the use of a rich, unhomogeneous culture? These questions will be discussed presently. Provisionally, the term "index of attracted bacteria" is useful to designate the figure obtained by comparing the number of leukocytes with

<sup>8</sup> Loc. cit.

<sup>9</sup> Loc. cit.

<sup>10</sup> In less than 3 per cent. of our examinations did this type of cells figure as phagocytes, and then only in small numbers—two or three to each count of 50 leukocytes.

<sup>11</sup> Jour. Amer. Med. Assoc., 1907, xlviii, 139.

adherent bacteria in diabetic and in normal bloods, using 1 as the normal standard.

In the following account of our experimental work we shall analyze the results according to these three groups of cases:

I. Diabetes mellitus.

II. Diabetes insipidus.

III. Non-diabetic glycosuria.

I. DIABETES MELLITUS. Of this affection 50 cases have been examined, all of which were undoubtedly true diabetes mellitus, as proved by the clinical history and by the urine analysis. In the 34 diabetics of the second series the frequency of the most prominent symptoms at the time of the blood examination may be tabulated thus:

	Per cent.	Cases.
Polyuria . . . . .	91.1	31
Abnormal thirst . . . . .	85.2	29
Wasting . . . . .	82.3	28
Excessive appetite . . . . .	70.5	24
Furunculosis . . . . .	52.9	18
Pulmonary tuberculosis . . . . .	29.3	10
Coma . . . . .	5.8	2

Glycosuria was found in all the patients, but in none was the sugar-content excessive, ranging from as low as 0.3 per cent. to as high as 3.4 per cent. This peculiarity was probably due to the fact that the great majority of the subjects were on strict diet and systematic medical treatment, either at the out-patient clinic or in the hospital ward. Acidosis was found in 44.4 per cent. (15 cases), and albuminuria in 41.4 per cent. (14 cases) of the patients examined. No lesion of the pancreas or of the liver was found in any of the patients.

In the foregoing group the opsonic index to *Staphylococcus* was determined in 50, while the indices to *Streptococcus* and to *Bacillus tuberculosis* were computed in the 34 patients of the new series only. In all the latter the values relating to phagocytized and attracted bacteria were also obtained. The information derived from this inquiry makes these conclusions inevitable:

(a) Diabetics, as a class, have subnormal *opsonic indices* to *Streptococcus*, *Staphylococcus*, and *Bacillus tuberculosis*, the diminution being most striking in tests made with the first-named bacterium, well defined with the second, and moderate with the last (Chart I).

As shown by Table I, the streptococcus index averaged 44 points below the accepted normal figure, ranging between 0.38 and 1.0, and falling below 0.5 in 7 tests. The staphylococcus index, although averaging 9 points higher than this, fell below 0.5 in 16 examinations; while the tubercle index, which averaged 17 points higher than the streptococcus value, fell below 0.5 but 3 times. Comparing the most common index-range of these three bacteria

(that is, 0.5 to 1.0), a much better conception of their relative values is possible, this analysis showing these averages:

Staphylococcus: 0.66, average index for 33 cases.  
 Streptococcus: 0.66, " " " 29 "  
 Tubercle bacillus: 0.65, " " " 24 "

TABLE I.—ANALYSIS OF THE INDICES IN 50 CASES OF DIABETES MELLITUS.<sup>12</sup>

	Opsonic Index.			Phagocytic Index.			Index of Attached Bacteria.		
	Staph.	Strep.	T. B.	Staph.	Strep.	T. B.	Staph.	Strep.	T. B.
Average . . . . .	0.65 <sup>13</sup>	0.56	0.73	0.74	0.64	0.70	0.50	0.47	0.59
Maximum . . . . .	1.44	1.00	1.73	1.18	1.04	1.33	2.64 <sup>14</sup>	3.00 <sup>14</sup>	8.30 <sup>15</sup>
Minimum . . . . .	0.25	0.38 <sup>16</sup>	0.45	0.25	0.11 <sup>16</sup>	0.20	0.16 <sup>16</sup>	0.10	0.10
Range of Indices.									
No. above 1.0 . . . .	1	0	2	3	1	2	3	1	1
No. 0.5 to 1.0 . . . .	33	26	29	26	26	25	6	10	7
No. below 0.5 . . . .	16	8	3	5	7	7	25	23	26

(b) The *phagocytic* and opsonin values are closely parallel with *Bacillus tuberculosis*, the former averaging 0.70 and the latter 0.73 in 34 experiments conducted with this germ (Chart II). With *Streptococcus*, however, the relation is not so close, averaging as 0.64 is to 0.56; and with *Staphylococcus* the breach is still wider—as 0.74 is to 0.65.

These departures of the phagocytic and the opsonic indices are most difficult to explain, although most of them can safely be referred to technical defects inherent to the tests. The propinquity of the bacteria to the cells, variations in the richness of the bacterial emulsion—not to mention personal errors in technique, apparently unavoidable—are doubtless often to blame. But such questions are not germane to our subject-matter, and their discussion must raise anew the controversy as to the relative value of the act of phagocytosis, and its result as gauged by the actual number of bacteria within the cells. In passing, it may be said that neither index should be considered a strictly quantitative guide, but a qualitative figure. The value of an opsonic index relates not to the precise figure registered thereby, but rather to the finding of a decided deviation from normal; and in the moderately subnormal ranges one may not hazard a definite conclusion, although at both extremes the readings are significant.

<sup>12</sup> Staphylococcus-index in 50 cases; streptococcus- and tuberculo-indices in 34.

<sup>13</sup> In 34 cases of second series—0.63 for average streptococcus-opsonin index.

<sup>14</sup> In 7 cases no attached bacteria observed.

<sup>15</sup> In 4 cases no attached bacteria observed.

<sup>16</sup> In 3 cases no phagocytized streptococci found; no attached bacteria.

(c) The *index of attached bacteria*, or those adherent to the periphery of the leukocytes, was studied with especial care in 34 bloods, in the hope of discovering some connection between this phenomenon and that of phagocytosis (Chart III). But the variations in our results were so wide that it is impossible definitely to associate the two processes: some actively phagocytic bloods contain leukocytes with no adherent bacteria whatever, while in others just the opposite

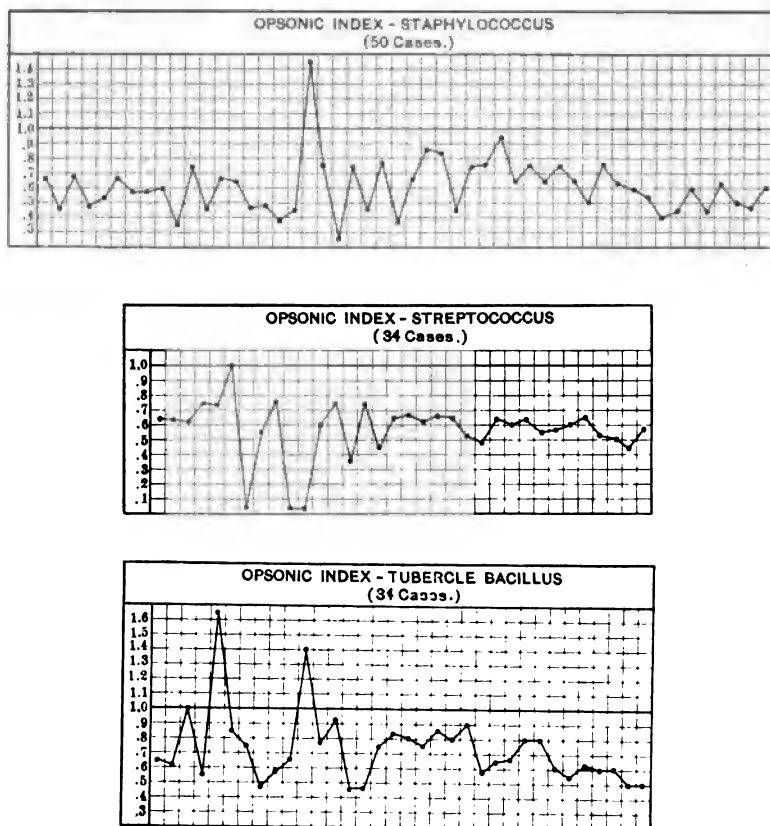


CHART I.—Opsonic indices in diabetes mellitus.

is observed. It is tempting to explain the former circumstance by assuming therein an extraordinary leukocytic defence, and the latter by assuming deficiency of this power, although it is saner to reject both hypothesis, leaving the question open to discussion. Three facts, however, were brought out by studying this detail of the attached bacteria: (1) That of the three different bacteria employed, tubercle bacilli were most frequently found clinging to the leukocytes, and, as a rule, doing so in far greater numbers than either strepto-

cocci or staphylococci; (2) that in the lower ranges (below 0.5) the uniformity of the index for all three bacteria was practically constant, differing, but very slightly, in favor of the tubercle bacillus; and (3) that to a somewhat less degree the same is true of the range of averages between 0.5 and 1.

The points referred to in the three preceding paragraphs are well illustrated by Table I, and in the accompanying charts the individual ranges of the three different indices are shown.

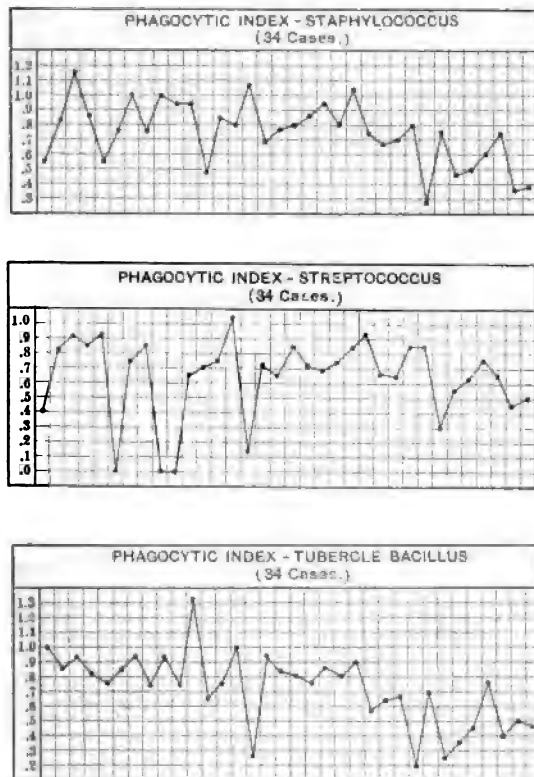


CHART II.—Phagocytic indices in diabetes mellitus.

(d) *Influence of Complications.* Thus far we have considered diabetics as a class, aside from which there remain numerous cases to be reviewed comparatively, owing to the existence of certain well-marked attendant or complicating conditions. To this class, then, belong those with acidosis, those suffering from furunculosis, and those affected with tuberculosis of the lungs.

In the group of *diabetes with acidosis* are included 15 patients whose urine contained acetone, diacetic acid, or both, in appreciable

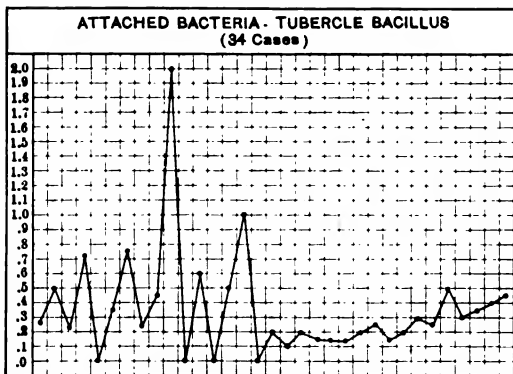
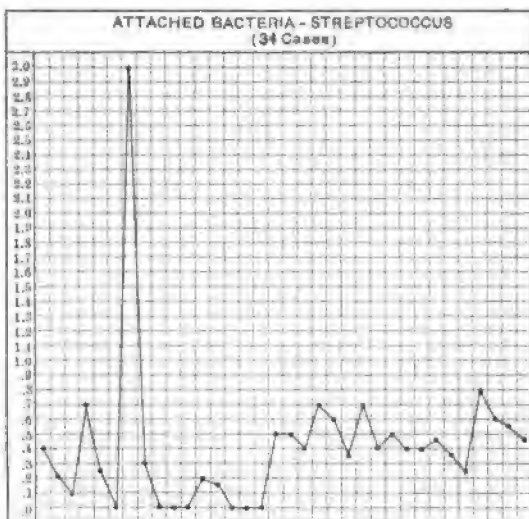
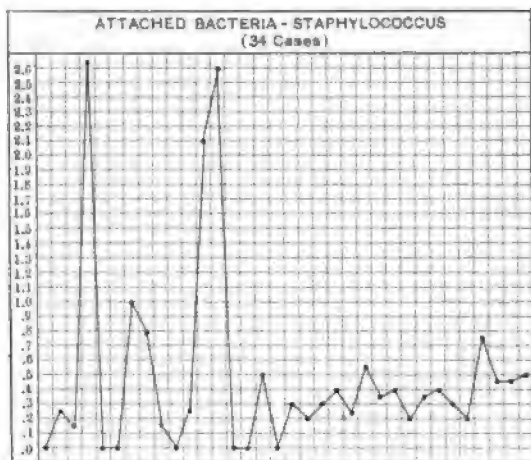


CHART III.—Indices of attached bacteria in diabetes mellitus.



amount at the time of the blood examination.<sup>17</sup> The term "acidosis" is used, therefore, in a somewhat loose sense, rather than necessarily to denote frank acid intoxication, perhaps amounting to coma, which was present in but two instances.

In dealing with this class of examinations one is forcibly impressed with two findings: the unduly low tubercle indices, both opsonic and phagocytic, in comparison with similar figures for cases without acidosis; and the virtually constant correspondence of the streptococcus and staphylococcus values in the two groups of patients.

Thus, the tuberculo-opsonic index averaged 23 points lower, and the tuberculophagocytic index 19 points lower, in acidosis cases than in the non-acidosis class. Even the questionable index of attracted bacteria declined in a most extraordinary degree—62 points for tubercle, and from 30 to 40 for the other bacteria. With reference to these findings it is important to note that but 2 of the low tuberculo-indices were found in tuberculous subjects affected with acidosis (Cases XXV and XLVII), and in neither was the value of such a nature as materially to affect the averages calculated for the complete acidosis series. In contrast to these deviations, the acidosis group of opsonic and phagocytic indices to the pyogenic cocci closely agreed with like values for patients without acidosis, the two differing not more than 4 points, save in the streptococcus phagocytic index, which ran 10 points lower in the acidosis class.

Of the 2 patients with *diabetic coma*, the urine of the first (Case III) contained both acetone and diacetic acid, and the urine of the second (Case XV) only acetone. In the first instance the opsonic values were 0.44, 0.61, and 0.51 to *Staphylococcus*, *Streptococcus*, and *Bacillus tuberculosis*, respectively; while in the second instance the corresponding values read 0.77, 0.45, and 0.46. In both patients the disease was of the acute type, and in the first one it proved fatal within a fortnight after the subject first came under observation.

This table of averages in diabetes with and without acidosis is illustrative of the decided differences here existing.

TABLE II.—DIABETES MELLITUS WITH ACIDOSIS.

	19 cases without acidosis. <sup>18</sup>	15 cases. with acidosis.
<i>Opsonic index.</i>		
<i>Staphylococcus</i> . . . . .	0.59	0.63
<i>Streptococcus</i> . . . . .	0.63	0.60
<i>B. Tuberculosis</i> . . . . .	0.89	0.66
<i>Phagocytic index.</i>		
<i>Staphylococcus</i> . . . . .	0.82	0.80
<i>Streptococcus</i> . . . . .	0.74	0.64
<i>B. Tuberculosis</i> . . . . .	0.86	0.67
<i>Index attached B.</i>		
<i>Staphylococcus</i> . . . . .	0.71	0.30
<i>Streptococcus</i> . . . . .	0.63	0.33
<i>B. Tuberculosis</i> . . . . .	0.92	0.30

<sup>17</sup> Lieben's and Gerhardt's tests were used in the routine examinations for acetone and diacetic acid, respectively.

<sup>18</sup> *Staphylococco-opsonin* index in 35 cases; all others in 19.

*Furunculosis* was present in 18 of the diabetic subjects, but, aside from certain minor details, this complication seems, *per se*, to have no material effect upon either the opsonic or the phagocytic power of the blood. In furunculosis cases, as well as in those with a clean skin, these averages were not dissimilar, save for a relatively feeble phagocytic action toward the staphylococcus and a comparatively vigorous attack upon the streptococcus, in the former group. In all the experiments it appeared that the combative powers of the leukocytes outstripped their destructive capacity for the bacteria attacked, since the phagocytic index consistently ran somewhat higher than the opsonic figure. The low range of the tubercle index of attached bacteria (45 points subnormal) is here almost as conspicuous as in the acidosis group. Table III demonstrates this peculiarity, as well as the other details just described.

TABLE III.—COMPARATIVE AVERAGE VALUES IN DIABETICS WITH AND WITHOUT FURUNCULOSIS.

	18 diabetics with furunculosis.	16 diabetics without furunculosis.
<i>Opsonic index.</i>		
Staphylococcus . . . . .	0.62	0.59
Streptococcus . . . . .	0.59	0.52
B. Tuberculosis . . . . .	0.69	0.77
<i>Phagocytic index.</i>		
Staphylococcus . . . . .	0.67	0.82
Streptococcus . . . . .	0.73	0.53
B. Tuberculosis . . . . .	0.71	0.78
<i>Index attached B.</i>		
Staphylococcus . . . . .	0.50	0.51
Streptococcus . . . . .	0.40	0.55
B. Tuberculosis . . . . .	0.36	0.91

Apropos of the above results (Table III), it may be noted that in 4 non-diabetic patients with furunculosis the opsonic index to *Staphylococcus* averaged only 0.45; while in 8 cases of pustular acne (also non-diabetic) the average indices were 0.50, 0.95, and 1.03 to *Staphylococcus*, to *Streptococcus*, and to *Bacillus tuberculosis*, respectively. These data, although limited, emphasize the great decline of the tuberculo-indices in diabetes complicated by furunculosis, in comparison with similar values found in non-diabetic persons affected with pustular lesions.

In *diabetes complicated by pulmonary tuberculosis* both opsonic and phagocytic indices averaged practically the same as those of non-tuberculous diabetics, except for a five-point and a twelve-point variation with the streptococcus. This can probably be disregarded, in view of the trifling differences involved, and because of the consistent uniformity of the other estimates. It is of some interest to find that in tuberculous diabetics the tuberculo-index of attached bacteria falls as it does in acidosis cases, although the average decline is some 11 points less than in the latter. The behavior of the several index averages in tuberculous and non-tuberculous patients is shown by Table IV.

TABLE IV.—DIABETES MELLITUS WITH PULMONARY TUBERCULOSIS.

	24 non-phthis- ical cases. <sup>19</sup>	10 phthisi- cal cases.
<i>Opsonic index.</i>		
Staphylococcus . . . . .	0.62	0.61
Streptococcus . . . . .	0.55	0.60
B. Tuberculosis . . . . .	0.73	0.75
<i>Phagocytic index.</i>		
Staphylococcus . . . . .	0.74	0.74
Streptococcus . . . . .	0.62	0.74
B. Tuberculosis . . . . .	0.68	0.69
<i>Index attached B.</i>		
Staphylococcus . . . . .	0.49	0.54
Streptococcus . . . . .	0.42	0.60
B. Tuberculosis . . . . .	0.71	0.41

(e) *Influence of Glycosuria.* The relation between the *degree of glycosuria* and the opsonophagocytic action was investigated in every case belonging to the second series, of which 18 had a sugar-content below 5 grains to the ounce, while in 16 this figure was exceeded, the average amount of sugar being 2.1 grains in the first, and 8.3 grains in the second, group.<sup>20</sup> Comparison of these groups admit of but one deduction: that a *high* degree of glycosuria implies a *low* grade of bacterial resistance, while with a moderate glycosuria the index is unquestionably higher. This is emphatically true of the tuberculo-indices, which in patients with a low sugar content showed an opsonic index 29 points higher, and a phagocytic index 33 points higher, than the corresponding value for subjects having a high content of sugar.<sup>21</sup> And here, as in the other cases referred to, the peculiar behavior of the tubercle index of attached bacteria attracts attention, for this value differs no less than 39 points in favor of the "low sugar" group of patients.

TABLE V.—INFLUENCE OF GLYCOSURIA ON THE INDICES.

	18 low sugar cases. <sup>22</sup>	16 high sugar cases. <sup>23</sup>
<i>Opsonic index.</i>		
Staphylococcus . . . . .	0.66	0.62
Streptococcus . . . . .	0.69	0.55
B. Tuberculosis . . . . .	0.89	0.60
<i>Phagocytic index.</i>		
Staphylococcus . . . . .	0.82	0.76
Streptococcus . . . . .	0.78	0.64
B. Tuberculosis . . . . .	0.93	0.60
<i>Index attached B.</i>		
Staphylococcus . . . . .	0.45	0.64
Streptococcus . . . . .	0.64	0.36
B. Tuberculosis . . . . .	0.81	0.42

<sup>19</sup> Staphylococco-opsonin index in 40 cases; all others in 24.<sup>20</sup> Fehling's and Böttger's tests were used for glucose, and in doubtful reactions, the fermentation and the phenylhydrazin tests.<sup>21</sup> The adjectives "low" and "high" here refer to the two degrees of glycosuria above alluded to—those below and those above 5 grains to the ounce.<sup>22</sup> Four cases with acidosis.<sup>23</sup> Seven cases with acidosis.

So far as we were able to determine, *albuminuria* is not to be regarded as a factor of index deviations. Nor could any correspondence be recognized between the *leukocyte count* and the phagocytic activity of the cells.

II. DIABETES INSIPIDUS. In 4 cases of diabetes insipidus opsonic indices of 0.82, 0.82, 0.87, and 0.89 to *Staphylococcus* were found, or values ranging within normal limits, which vary from 0.80 to 1.2, according to Bulloch's studies of 84 healthy subjects.<sup>24</sup> The foregoing cases belong to the first series reported, in which only the staphylococco-opsonic index was investigated, and having met with no more examples of this disease during the past year, we are denied the opportunity of recording the behavior of the phagocytic percentage and the index of attached bacteria in non-saccharine diabetes. On clinical grounds, it is unlikely that there is any deviation from normal, although no actual proof of this presumption is at hand.

III. NON-DIABETIC GLYCOSURIA. In 8 patients with transient glycosuria all the index values, collectively and individually, were well within the normal range, except in the last 3 tests with *Streptococcus*, which showed moderately subnormal opsonic indices (0.70, 0.76, and 0.75), with most divergent values for phagocytes. This we regard as a discrepancy due to the use of an unsatisfactory streptococcus culture, with which bacterium, it may be added, we have had considerable trouble at different times. This being the case, we prefer to draw no conclusions from the streptococcus values in the cases under discussion, and figures relating to this germ are stated with this proviso.

With the other bacteria consistently high values were obtained, ranging some 20 to 30 points higher than similar values for diabetes mellitus. Although 8 records are scarcely comparable with 50, we tabulate the averages of non-diabetic glycosuria with those of diabetes mellitus, in view of the striking contrast thereby shown.

TABLE VI.—GLYCOSURIA VERSUS DIABETES.

	8 glycosuria cases.	50 diabetic cases.
<i>Opsonic index.</i>		
<i>Staphylococcus</i> . . . . .	0.96	0.65
<i>Streptococcus</i> . . . . .	0.81 (?)	0.56
<i>B. Tuberculosis</i> . . . . .	0.98	0.73
<i>Phagocytic index.</i>		
<i>Staphylococcus</i> . . . . .	1.01	0.74
<i>Streptococcus</i> . . . . .	1.02 (?)	0.64
<i>B. Tuberculosis</i> . . . . .	0.93	0.70
<i>Index attached B.</i>		
<i>Staphylococcus</i> . . . . .	0.79	0.50
<i>Streptococcus</i> . . . . .	0.62 (?)	0.47
<i>B. Tuberculosis</i> . . . . .	0.54	0.59

<sup>24</sup> Trans. Path. Soc., London, 1905, lvi, 234.

**CONCLUSIONS.** With no sacrifice of logic, we believe that the following deductions are warranted by the clinical and laboratory findings herewith reported:

1. In diabetics, as a class, the resisting powers of the blood against bacterial infection are conspicuously subnormal, in comparison with a similar hemic property in the healthy individual. As measured by the opsonic index, the average diabetic's resistance is approximately one-third below normal, and, in the exceptional case, reduced more than two-thirds. This applies to infections by the streptococcus, the staphylococcus, and the bacillus of tuberculosis, whose relative predilection for the diabetic is expressed by the order given.

2. The higher grades of diabetic glycosuria are attended by a feebler opsonophagocytic action than the lower grades, and the reverse of this also is true. This deficiency is particularly striking in the case of the tubercle bacillus.

3. Diabetic acidosis particularly lowers the blood resistance to the bacillus of tuberculosis, but a less degree of vulnerability appears to exist with regard to the streptococcus and the staphylococcus.

4. Diabetic furunculosis does not materially depress the subject's opsonophagocytic powers to the ordinary pyogenic cocci below the figures usually incident to this disease.

5. Diabetics affected with pulmonary tuberculosis show virtually the same resisting powers as do subjects of uncomplicated diabetes.

6. In non-saccharine diabetes the opsonic values to the staphylococcus range within normal limits, and this statement also applies to non-diabetic glycosuria.

In conclusion, we would advise the use of the opsonic test in diabetes mellitus as a means of gaging, in a general way, the extent to which the subject's vitality is undermined, and for this purpose the test is especially useful in patients threatened with acid intoxication, and in those having excessive glycosuria. Systematic opsonic records in an average case of diabetes reflect most clearly the inroads of this affection, as well as the patient's behavior under the stress thereby imposed. Of this we have ample proof, in numerous patients in whom repeated examinations were made, over extended periods of time. In this connection also, the opsonin test, hitherto studied only in its relation to infectious processes, should be useful in the investigation of several other conditions—gout, rickets, jaundice, and cachexias consequent to chronic nephritis, hepatic cirrhosis, malignant disease, and severe anemia.

## THE BLOOD PRESSURE IN ARTERIOSCLEROSIS.

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It has long been known that in cases of thickened arteries the blood pressure is likely to be raised. This increased pressure used to be recognized only by the fingers of the examiner, and was referred to as the "tension between the beats." During the last few years, however, many instruments have been introduced for accurately measuring this pressure. Most of these measure not the tension between the beats at all, but the force of the pulse wave, or, as it is termed, the "systolic pressure." A few, such as that of Erlanger, gauge the pressure between the beats, or, as it is called, the "diastolic pressure;" but most work has been done upon the systolic pressure, which is practically the force of the left ventricle. P. M. Dawson<sup>1</sup> has shown conclusively that the best measure of the systolic output of the heart is the pulse pressure, that is, the difference between the diastolic pressure and the systolic pressure. A patient may have an abnormally high systolic pressure and yet have a dangerously low pressure between the beats, as was the case in a woman examined recently who was dying of aortic regurgitation and yet her systolic pressure was 170 mm. Hg.; her still abnormally strong heart was pumping blood into a comparatively empty arterial tree.

My work has been mostly done with the Martin and the Janeway sphygmomanometers, both of which are modifications of the Riva-Rocci instrument. The former only registers the systolic pressure; the latter is supposed to give also the diastolic pressure, but in my hands at least is very unsatisfactory in this respect. I venture to express the belief that it is the diastolic pressures that we most require to know, and I think that there is great need of a portable instrument that will meet this want.

Although the sphygmomanometer is often of the greatest value in making accurate measurements of blood pressure, the importance of estimating the blood pressure—both systolic and diastolic—by the trained finger is as great as ever, and in many cases is all that is necessary. In the majority of cases, with a little practice, one can even come very near to the systolic pressure in millimeters of mercury by the trained touch alone. The cases in which one is most likely to err are those of very high pressure; it is very difficult, for example, to measure the pressure of a pulse above 200 mm. In arteriosclerosis the first rise that may occur is in the pressure between the beats, and the left heart, as a consequence, becomes stronger than normal, and its amount of hypertrophy is a good gauge of the degree of pressure that it has had to work against.

<sup>1</sup> Brit. Med. Jour., October 20, 1906.

At one time increased arterial pressure was spoken of as a constant accompaniment of arteriosclerosis, but now that actual measurements can be made, it is found that frequently this pressure is normal or even below normal in such cases. Dunin<sup>2</sup> measured the blood pressure 1000 times in 440 patients with arteriosclerosis in his private practice. He used Gaertner's tonometer in his work. In 120 out of the 440 arteriosclerotic people (27.5 per cent.) the pressure was normal or low. Groedel,<sup>3</sup> of Nauheim, recently published measurements in 500 cases of well-marked arteriosclerosis. In 35 per cent. he found no increase in pressure. Many other workers have come to the same conclusion, and as far as one's small experience warrants, the conclusion is the correct one. Last winter Messrs. A. Ellis and L. B. Robertson, senior medical students in the University of Toronto, investigated this point for me in the General and St. Michael's Hospitals, and their results show that only in about half of the well-marked cases of arterial thickening examined did the pressure run above normal. Occasionally we find a low pressure, when, from the enlargement of the left heart, etc., it is evident that at last the heart is giving up its struggle against long-continued, high pressure. Such a case as the following illustrates this point: A tall, thin man came complaining of great dyspnoea and other signs of cardiac insufficiency. His vessels were markedly thickened and tortuous, and the cardiac apex was felt in the sixth left intercostal space outside the nipple line, and yet the pulse could scarcely be distinguished at the wrist. He was near his end.

Granting that there are many cases of well-marked arteriosclerosis in which the blood pressure is at or below normal, and apparently has never been otherwise, how can we account for the apparent discrepancy? It must be remembered that it takes a great deal of interference with the arterial tree before there is any alteration in the general blood pressure. One may, for example, ligate a large artery, such as the femoral or the common carotid in the dog, without producing any long-continued rise in the general pressure. It is probable that in many of the cases of well-marked sclerosis of the radials the pressure is not raised because the rest of the arterial tract is normal. Localized sclerosis of the splanchnic vessels, however, is said more easily to give rise to increased arterial pressure than is the same amount of disease elsewhere, these vessels being intimately connected with the regulation of the general blood pressure. Hasenfeld and Hirsch, according to Janeway,<sup>4</sup> have definitely proved that arteriosclerosis only leads to increased blood pressure and hypertrophy of the left ventricle when the splanchnic vessels or the aorta above the diaphragm are highly diseased.

<sup>2</sup> *Ztschr. f. klin. Med.*, liv, Nr. 4.

<sup>3</sup> T. Clifford Allbutt, *Brit. Med. Jour.*, October 20, 1906.

<sup>4</sup> *The Clinical Study of Blood Pressure*, p. 143.

During some experimental work on blood pressure done some time ago in the Physiological Department of the University of Toronto<sup>6</sup> I came to the conclusion that, while the splanchnic vessels are all-important in the maintaining of blood pressure, yet the vessels below that point are also of great value in the same way; and I should much like to hear of a case of marked sclerosis of the arterial tract below the origin of the splanchnic vessels, and with these vessels normal, in which there was a normal arterial pressure.

When, in a case of arteriosclerosis, we find the pressure to be high, it is necessary to find out how much of this hyperpyresis is due to the disease of the vessel walls and how much to other causes. Careful and repeated examinations of the urine will help toward finding if the condition is due in whole or in part to disease of the kidneys. There may be, and frequently is, a vasomotor element in the case due to toxic or nervous influences, and the free use of the nitrites will assist in gauging the amount of this factor present, the pressure falling much more in such cases than when the pressure is due solely to sclerosis of the vessel walls. Sir Clifford Allbutt<sup>7</sup> writes that "it is a remarkable experience that in cases of great involutionary deformity of the vessels, or, at any rate, of those that are palpable, intercurrent attacks of hyperpyresis may be detected, estimated, and dissipated with as much ease as in persons not so affected."

The question suggests itself here of how much of the normal pressure is dependent upon the activity of the suprarenal capsules. If these are normally active, other influences being undisturbed, the arterial pressure will remain normal. If, however, the suprarenals be sluggish, then the pressure should remain low, and, on the other hand, if they be overactive it should be raised. We know of variations in the functional activity of so many other glands of the body that the conclusion seems almost inevitable that in many cases of disturbed blood pressure we are dealing with examples of over- or under-activity of the suprarenal glands. This interesting question was very ably discussed by Dr. H. D. Rolleston<sup>7</sup> at the last meeting of the Canadian Medical Association, at Montreal.

On the whole, one may say that the finding of a heightened blood pressure is of some value in the diagnosis of a widespread arteriosclerosis, but that, on the other hand, a considerable and often very serious degree of the disease may exist with a normal pressure. I have studied many cases of the latter class in the last few years. One such case much impressed me recently. It was that of a professional man, aged forty-six years, who, after an abstemious but strenuous life, began at the age of forty-three years to suffer from angina pectoris. His right radial was markedly sclerosed, but not so the left or either brachial artery. The blood pressure, upon re-

<sup>6</sup> Observations on Blood Pressure, Univ. of Toronto Study, No. 3.

<sup>7</sup> Loc. cit.

<sup>7</sup> Canada Lancet, November, 1907.



peated examination between the attacks, never ranged above 145 mm. The urine was normal. He died in an anginous attack, and the post-mortem examination revealed very marked sclerosis of the coronary arteries, but little disease of the rest of the arterial tree. Another case comes to mind—that of a clergyman, aged sixty-three years, who died of slow cerebral thrombosis. His grandfather had died of apoplexy at seventy years, and the father at sixty-seven years of some similar condition. In this case the arteries open to palpation were not sclerosed beyond what is normal at sixty-three years and the blood pressure was not raised. He had lived a most abstemious life, except as regards "high thinking."

The rise in pressure in cases of sclerosis is usually attributed to the resistance to the onward flow of blood produced by the sclerosed arterial walls. But it is in some cases due possibly to quite a different mechanism. Kocher and Cushing showed some time ago that in localized anemic conditions of vital parts of the brain the blood pressure rises enormously, this rise being evidently an endeavor upon the part of the body to force blood into the dangerously blanched areas. Cook and Briggs<sup>\*</sup> also illustrate this well by a chart showing the blood pressure in a case of hemorrhage upon the surface of the brain. The pressure was 360 mm., and after the removal of the clot it fell and remained at normal. Recently a somewhat similar case came under observation: A lady, who had been well except for frequent headaches and some slight hesitation in speech, became for the third time this winter rather suddenly unconscious with signs of acute cerebral compression. During the attack her pressure rose from 125 to 210 mm. Next day, although still profoundly unconscious, with fixed pupils and Babinski's sign in both feet and other signs of marked pressure, her blood pressure was found to be 135 mm. This sign helped one to surmise that the cerebral compression was lessening, and within twelve hours she was quite conscious and is now practically well. These are illustrations of acute compensatory rises in blood pressure, but it seems altogether likely that if the circulation in vital parts of the brain is interfered with by arterial sclerosis, the general blood pressure will rise in the same way in order to get blood into the needful parts.

With the general treatment of arteriosclerosis one is not here concerned, but it may not be out of place to mention a few points from the blood pressure point of view. It is in what has been called the pre-sclerotic stage of the disease that most may be done to relieve the condition. One would fully endorse Sir Clifford Allbutt's sound advice that every adult of say forty-five years and over should, at intervals of two or three years, have his blood pressure taken, in the hope that it may guide his physician to use every endeavor to postpone or prevent the onset of arteriosclerosis. Not that an

<sup>\*</sup> Clinical Observations on Blood Pressure, Johns Hopkins Hospital Reports, 1903, vol. xi.

increased pressure will inevitably produce sclerosis, although if continued long enough and be high, it may do so, but increased pressure and damage to the vessel walls may both be due to some toxin that can, by careful living and treatment, be lessened. In such cases, if we adopt measures such as restricted diet, increased elimination, and the use of the iodides, we may keep the pressure down and are probably at the same time lessening the toxemia which will soon lead to irritation and consequent sclerosis of the vessel walls. It is not advisable in every case of arteriosclerosis immediately to resort to strong measures, such as the nitrites, in order to lower an abnormally high blood pressure. The tissues supplied by the thickened arteries, and it may be vital tissues, are only able to get enough blood for their uses when the pressure is abnormally high.

It is wonderful what apparently good health many of these arteriosclerotic people enjoy, even when their pressures are very high. Such a case as the following is of every-day occurrence: A lady, aged fifty-eight years, feels well, except for some breathlessness on exertion and an occasional sense of oppression in the chest. The urine is normal and the arteries moderately sclerosed. Her systolic pressure is constantly between 220 and 235 mm. She has an occasional numbness in the left arm and frequently is dizzy, but does not suffer from headaches. In my experience headaches are not common in arteriosclerotic cases in which the urine remains normal, and I note with interest that G. L. Walton and W. E. Paul<sup>9</sup> recently found, in an analysis of 100 cases of arteriosclerosis, that headache was only present in 22 per cent.

Arteriosclerotic patients often feel weak and shaky and, with the idea of keeping up their strength, take more food than they would use in health. Such a patient came to me about three years ago. Her blood pressure was 240 mm. She was nervous, depressed, and suffered from some headache, and, with the wrong idea that the condition was due to want of nourishment, was taking three good meals a day with lots of meat and eggs, and between meals frequent cups of strong beef tea and sips of whisky. Under a restricted diet, with free saline laxatives and small doses of iodide of potassium, her pressure came down to 190 mm., and she felt much better and the desire for extra food left her. She kept thus fairly well until last month, when she had a hemiplegic attack, and then the urine for the first time was found to be albuminous and the blood pressure over 200 mm.

The onset of early arterial sclerosis should be specially looked for and as far as possible prevented in those individuals whose family history shows that they have a tendency to the disease. Personally, I have seen more cases of the disease in those who have lived abstemious lives than in those who have indulged too freely in the

pleasures of the table. In many such cases the only fault that can be found is the strain and stress of modern life acting upon individuals in whom, as Osler graphically puts it, bad material was used in the make-up of the vascular machine.

CONCLUSIONS. 1. In many cases of even well-marked arteriosclerosis the blood pressure is not raised. This may be because the disease is localized to a part of the arterial tree, or because the heart may at last be giving up the struggle and hence the pressure, once high, has now fallen.

2. In many cases of arteriosclerosis the blood pressure is above normal.

3. In a given case of arteriosclerosis, in which the pressure is found to be raised, it cannot be assumed that the pressure is high because of the disease of the vessel walls, nor yet that the sclerosis is due to the increased pressure. For example, the arterial stiffening may be due to syphilis, and the hyperpyrexia to some intercurrent condition of nervous or toxic nature which may be more or less removable by appropriate treatment.

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### **SYMPTOMS ATTRIBUTED TO THE MYOCARDIUM IN REALITY OFTEN OF PERIPHERAL ORIGIN.**

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THE progress of medical thought has always been one of differentiation whereby a group of symptoms which at the time stands for a supposed entity is after a while divided to represent two different conditions, and these are again subdivided, until finally, in place of one disease with a very complex group of symptoms, there is a number of simpler ones with fewer symptoms. Thus, typhus fever once covered typhoid fever, what is now known as typhus fever, and a number of other febrile conditions which have since been more definitely placed. Rheumatism also has been differentiated into a good many conditions which now present no difficulties of distinction.

The same thing is about to happen to that group of heart conditions which has been called myocarditis, corresponding to a predicated organic disease of the heart muscle, which was supposed to produce certain symptoms. It has been customary to attribute many sudden deaths to this condition, while, in fact, it is not logical to believe that a disease characterized by destruction of muscular tissue should terminate suddenly without previous manifestation of muscular weakness. I should be willing once for all to rule out

from the group of pure myocardial disease all those cases in which there is no sign of myocardial weakness, as shown by the inability of the heart to develop extra muscular force, when such force is needed; in other words, cases in which action of the heart responds to the demands of exercise, in which there is no dyspnoea when the physiological activities of the body are increased, as during digestion, or at night when the blood tension is higher, and those cases in which there is no failure of the proper circulation of the blood in any part of the body, not even the liver, which is often the first to suffer.

Again, I should rule out as true myocarditis those cases in which there have been gross departures from normal in the peripheral circulation, such as extreme high tension that has led to hypertrophy and exhaustion of the heart muscle, for in these cases, when relieved of the outside attacks upon its integrity, the heart muscle often shows wonderful recuperative powers. Again, I should like to express the belief that in the undoubted cases of myocardial degeneration due to infectious diseases, many of the symptoms are really due to a coincident degeneration of the peripheral vasomotor mechanism, and if this can be regulated the heart muscle will be found quickly to regain a sufficient tone to answer reasonable demands. In diphtheria particularly the well known tendency of the toxin to attack the nervous mechanism makes it seem more than likely that the muscular fibers of the heart may after all not be the most important elements involved. The heart muscle is one of the most tolerant structures in the human body, and has carried the odium of many accidents which never belonged to it.

I do see a certain number of cases which seem to me to be true myocarditis, but as my attention has been more and more drawn to the circulation as a whole, not neglecting its peripheral vessels and nervous control, these cases have become fewer and fewer. The name arteriosclerosis, taken in its broader, modern sense of disorder of the bloodvessels (the best name we have, but not a good one), would more truly cover many cases that have been attributed to myocarditis. An individual who has been subject to general toxic conditions, disease, indiscretion of diet, or some specific poison or intoxication, is found with a pulse irregular in force and rhythm, attacks of dizziness, and perhaps tinnitus. The heart is free from murmurs, there is no particular dyspnoea on exertion, the arterial tension is low, there is no congestion of the liver and no oedema of the extremities. Such a case I believe to be ordinarily a case in which the true lesion is to be found principally in the circulatory mechanism located in the nerves and vessels outside of the heart.

On the other hand, a patient shows the same irregularity, or perhaps no irregularity at all, in the pulse, hypertonicity of the bloodvessels (through an attempt of the vessels to compensate for the weak heart), congestion of the liver, dyspnoea on exertion, slight oedema of the feet; I should not hesitate to say that that patient

is suffering from a true weakness of the heart muscle. So I must confess that a study of the circulatory disease has led me almost to a reversal of my original conception of the symptomatology of myocarditis. This train of thought, principally started by the apparent inconsequence of the outcome of these cases, and continued later by reflection on the results of the experimental destruction of the heart muscle as observed in the experimental laboratory and on the relation of blood pressure study in these cases, has made me prepared at the present time to change my views.

There is something more to be learned as to blood pressure in its relations to vascular tone and the movement of blood in the vessels, and I hope the time will soon come when we shall be prepared to make a better classification of blood pressure symptoms. To this end the routine use of the sphygmomanometer, while not allowing its findings to cover the whole surface of the clinical picture, is important.<sup>1</sup>

A true myocarditis with its characteristic symptoms is seen in acute syphilitic inflammation of the heart muscle. In such cases, with absolute irresponsiveness of the heart muscle to physical and physiological demands, may be found the fundamental symptoms of myocarditis. When the heart sounds can be heard satisfactorily, murmurs are likely to accompany myocarditis. Murmurs arise so quickly from dilatation of one part or another of the heart, such as logically exist if the heart muscle is markedly deficient, that it is difficult to believe in the existence of myocarditis where the sounds of a forcibly acting heart are present without murmurs, although some very recent writers believe in such myocarditis.

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## PERSISTENT PATENCY OF THE DUCTUS ARTERIOSUS.

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PERSISTENT patency of the ductus arteriosus has been the topic of several extensive articles, but in reviewing the literature in connection with the study of a case that I recently had the fortune to examine postmortem, it was found that there is practically no systematic discussion of the topic in the English literature, and that none of the reports is complete in the light of recent developments. Therefore, although the occurrence of a patent ductus arteriosus in an adult, which gives rise to symptoms during life and is demonstrated at

<sup>1</sup> In these studies I now use the hydrostatic instrument, which will be found described in the appendix (1908) of Wood's Reference Handbook of the Medical Sciences, in the article on "Arteriosclerosis."

autopsy, is of itself so uncommon as to call for study and publication, it would seem also to be desirable to review rather completely the entire subject as it stands at the present time. Among the best systematic discussions are those of Rauchfuss<sup>1</sup> (1859), Gerhardt<sup>2</sup> (1867), Wraný<sup>3</sup> (1871), Vierordt<sup>4</sup> (1898), and Gérard<sup>5</sup> (1900); but since the first three of these were written the work of Zuntz<sup>6</sup> and Strassman<sup>7</sup> seems to have explained satisfactorily the mechanism of the normal closure of the ductus arteriosus and to have thrown an entirely new light upon the subject, while in the articles of Vierordt and Gérard this work is not taken into account. Later articles in which the studies of Zuntz and Strassmann have been considered, by Roeder<sup>8</sup> (1900) and Wagener<sup>9</sup> (1903), are particularly concerned with certain features of this subject and do not discuss it in a comprehensive manner.

The case that I have to report concerns a patient in the service of Dr. Charles Mix at the Cook County Hospital. The history is obtained from the notes of the internes, Drs. Moes and Grisinger, in whose charge he was. The man was aged forty-two years, born in Sweden, and occupied as a general laborer in a piano factory. He entered the hospital on account of severe icterus and pronounced cholemic manifestations, which suggested the possibility of the presence of occlusion of the common duct by a malignant growth. This cholemic condition persisted during the eight days he was under observation before death, and as the liver seemed to be small, and it was found that there was no constant obstruction to the entrance of bile to the intestine, acute yellow atrophy was suspected. Death occurred on July 10, 1907, after a sudden rise of temperature to 106°, and some hemorrhage from the bowel.

The previous history of the patient was negative; he denied any previous illnesses, and apparently had never been in any way affected by the condition of the heart and vessels, at least not enough to attract his attention to them. The cause of the death of his parents was unknown; he had one brother and one sister living and well. He admitted drinking considerably of both alcoholic and malt liquors. Examination of the heart at the time of entrance was made, and the notes on the history sheet are as follows: The apex beat is diffuse as seen and felt in the sixth interspace just inside the nipple line. The area of cardiac dulness reaches to the upper border of the fourth rib above and a finger's breadth outside the

<sup>1</sup> Virchow's Archiv, 1859, xvii, 376.

<sup>2</sup> Jena Zeitschr. f. Med. u. Naturwissenschaft., 1867, iii, 105.

<sup>3</sup> Oesterreichsches Jahrb. f. Pädiatrik., 1870-1871.

<sup>4</sup> Nothnagel's System, 1901, xv, Pt. 2, 155.

<sup>5</sup> Revue de méd., 1900, xx, 845 and 837; Jour. d. l'Anat. et Physiol., 1900, xxxvi, 1 and 323; 1903, xxxix, 1.

<sup>6</sup> Pfüger's Archiv, 1888, xlii, 342.

<sup>7</sup> Arch. f. Gynäkol., 1894, xlv, 393.

<sup>8</sup> Arch. f. Kinderheilk., 1900, xxx, 157; Virchow's Archiv, 1901, clxvi, 513.

<sup>9</sup> Deut. Arch. f. klin. Med., 1903, lxxix, 90.

nipple line, with impaired percussion note to the anterior axillary line; it reaches the right border of the sternum to the right. The impulse is very strong in the apical region, and "it almost seems as if there were a thrill there." The sounds at apex are very loud, and the first sound is impure. A murmur is heard in the second right interspace which is quite loud and blowing, systolic in time, and also heard in the second and third left interspace; the second sound is accentuated. The heart misses a beat at long intervals. A note by another examiner two days later also notes the murmur in the second right interspace, and records the absence of any palpable thrill. Two days before death the following note was made: Dulness extends one inch to the right of the sternum in the second interspace; a systolic murmur is heard here, and down along the right border of the sternum; the second sound is accentuated; there is no thrill; the heart beats are rather forcible. A distinct systolic murmur is heard in the sixth left interspace.

As can be seen, the predominant feature in this case was the icterus and cholemia, the cardiac findings being secondary; these were, however, such as to impress the examining physicians as being different from the ordinary heart lesions, and a tentative diagnosis of dilatation of the aorta was made. As will be seen later, the dulness in the right second interspace is a prominent feature of patency of the ductus arteriosus, and the murmur as heard was of a suggestive character.

A summary of the findings at the autopsy follows:

The body is that of a small, fairly well nourished and developed man, extremely icteric. There are several small subcutaneous lipomas on the right forearm. The abdominal cavity shows no changes except for a small left inguinal hernia. The diaphragm is at the normal level. The liver is three fingers' breadth above the costal margin, its size considerably decreased, the weight being but 1100 grams; it is a deep yellow color, consistence flabby, and there are numerous subperitoneal ecchymoses. The gall-bladder is moderately distended, all the large ducts are patent, and there are no concretions. The cut surface of the liver is very yellow, and there is an evident increase in the connective tissue about the lobules. Microscopically there was found in this liver a pronounced multilobular cirrhosis, with severe icterus and icteric necrosis, plus fatty changes. The lungs show subpleural hemorrhages and moderate atrophic emphysema. Gastro-intestinal tract shows no abnormalities except a small diverticulum in the œsophagus 8 mm. in diameter and 4 mm. deep, located in the anterior wall just below the bifurcation of the trachea; there are no evidences of adhesion of the external wall of the œsophagus to the surrounding tissues at this point. The large intestine contains feces that are clay colored. The kidneys are enlarged, weighing 460 grams, are much stained with bile; cortex 8 mm. thick; capsule strips easily, occasionally tearing off

strips of cortex. In the spleen, which is embedded in adhesions, are many scars of healed anemic infarcts.

The heart weighs 360 grams, being slightly enlarged. The valves are all normal, and the size of the orifices is normal. There are numerous small subendocardial ecchymoses. Foramen ovale closed; interventricular septum normal. The beginning of the aorta is of normal diameter, and there is but slight sclerosis of the aorta, although the smaller arteries of the heart and throughout the body are considerably sclerosed. The wall of the



FIG. 1.—Patent ductus arteriosus. The black rod passes into the opening of the duct in the aorta, about which the sclerotic patches can be seen. The external surface of the duct is seen in its course to the segment of the pulmonary artery, the external surface of which is shown in the photograph. (Natural size.)

left ventricle is of normal thickness, while the right ventricle is slightly thickened. Pulmonary artery not sclerotic. At the normal location of the arterial ligament there is a duct-like communication between the aorta and the pulmonary artery, the patent ductus arteriosus (Fig. 1). The upper margin of the opening of the duct into the aorta is located about 5 mm. below the level of the lower margin of the left subclavian artery; at this point the lining of the aorta shows a slight transverse striation with apparently slight thickening of the subendothelial connective tissue. Here the internal



circumference of the aorta (hardened in alcohol) is 37 mm., while 2 cm. lower down the circumference is 45 mm. The length of the duct from the margin of the aortic opening to the pulmonary orifice is 16 mm. The aortic orifice is elliptical in shape, the greatest diameter is transverse of the aorta and measures 8 mm. The pulmonary orifice is bounded by a ring of thickened intima 5 mm. in diameter, from which projects a mound-like elevation, symmetrical, 1.5 to 2 mm. high, apparently formed by a proliferation of the margins of the orifice (Fig. 2). These folds are quite pliable, about as thick as the thickest part of a normal aortic valve. The opening of the duct is situated at the top of this mound, circular in outline,

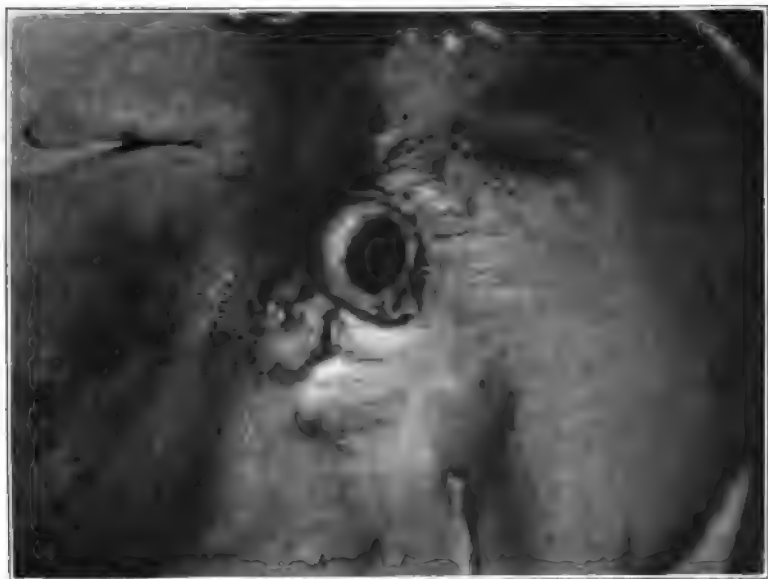


FIG. 2.—The opening of the duct into the pulmonary artery, at the summit of a mound-like protrusion of the intima of the pulmonary artery. (Magnified three diameters.)

and measures 2 to 3 mm. in diameter. Although the aorta itself is nearly free from sclerosis, at the opening of the duct is a sclerotic patch 16 mm. long, 7 mm. broad, about 1 mm. thick, calcified into an elliptical plaque. This stretches across the lower margin of the aortic opening of the duct, transverse to the long axis of the aorta. The duct itself is in the form of a rigid, cylindrical tube, the external diameter averaging 10 mm. Its lumen shows an extremely sclerotic appearance, and the diameter of the cavity is quite uniform, about 6 mm., until the point of insertion of the duct into the pulmonary artery is reached, where it narrows down quite abruptly to the size of the pulmonary orifice. There are no evidences of thrombosis or of aneurysmal dilatation.

The anatomical diagnosis was as follows: General icterus; atrophy of the liver, with icteric necrosis and beginning atrophic cirrhosis; chronic parenchymatous nephritis; patent ductus arteriosus, with sclerosis of the ductus; atrophic pulmonary emphysema, with multiple ecchymoses in the lungs; fatty degeneration of the myocardium; healed infarcts in the spleen, with fibrous perisplenitis; multiple subcutaneous lipomas; diverticulum of the œsophagus; general arteriosclerosis.

To summarize, the condition of the patient's vessels had apparently nothing to do with his final illness, which was probably a catarrhal jaundice in a person with atrophic cirrhosis and parenchymatous nephritis. The patency of the ductus arteriosus had not led to any considerable effect upon the heart, except for a very slight thickening of the right ventricle; it is possible that the healed infarcts in the spleen were due to emboli coming from the ductus at some previous time, as there was no other apparent source for them. Clinically the patency of the duct had led to distinct physical findings, but does not seem to have given rise to noticeable symptoms.

**OCCURRENCE OF PERSISTENT PATENCY.** Under normal conditions the ductus arteriosus ceases to be functionally patent, that is, to transmit blood from the pulmonary artery to the aorta, when the fully developed infant takes its first breaths. Complete anatomical closure, so that there is no lumen through which blood can find its way under any conditions, requires several days for its completion; in many perfectly normal babies the duct does not become impervious until from three to six weeks, although it usually closes much earlier, for Billard found only three in twenty still patent after eight days. Not rarely it happens that some part of the lumen remains open throughout life, and can be found in sections of the remnants of the duct, although complete impermeability exists at one or several points; not rarely a duct can be entered for some distance from one or the other end with a fine probe, and sometimes the probe may be forced completely through, but without the duct having been functionally patent. If we exclude these slight variations from the normal occlusion, and consider as instances of pathological persistence of patency only those cases in which the lumen of the duct has been free for the passage of blood during the life of the patient, the number of examples reported is small. It is to be emphasized that we are here considering only simple, primary persistence of the ductus arteriosus, for in nearly every form of congenital heart lesion and anomaly of the great vessels the ductus arteriosus remains patent, for reasons that will be discussed later; but in such cases the persistence of the duct is usually overshadowed by the other abnormalities, and the entire picture is quite different from the one under consideration.

In 1898 Vierordt stated that he could find but 26 authentic instances recorded in the literature, in which the existence of un-

complicated persistence of the ductus arteriosus was established by postmortem examination. These constituted but about 4 per cent. of all the recorded cases of congenital diseases of the heart and great vessels; thus the infrequency of this condition may be appreciated. Including cases not mentioned by Viero:dt, and additional cases reported since 1898, I have found 15 more, making a total of but 41. There are about half a dozen other probable cases in which I have been able to obtain only such incomplete records that they have not been incorporated in the following table:

Age.	Total cases.	Male.	Female.
Newborn . . . . .	5	1	2
1 to 3 months . . . . .	6	1	1
4 to 12 months . . . . .	1		
1 to 10 years . . . . .	5	2	2
11 to 19 " . . . . .	4	2	2
20 to 30 " . . . . .	5	2	3
31 to 40 " . . . . .	6	2	4
41 to 50 " . . . . .	6	2	4
51 to 60 " . . . . .	2		2
61 to 66 " . . . . .	1		1
Total . . . . .	41	12	21

If we consider only the cases in which the subject reached maturity, there are but 20, so that the condition present in the case reported herewith is indeed a rarity. However, it is certain that these figures give a very erroneous impression as to the frequency of persistent patency of the ductus arteriosus, for, in the first place, within the past few years there have appeared numerous reports of cases in which this diagnosis has been made clinically with a considerable degree of certainty, but without postmortem corroboration. Again, there is no doubt that very frequently the condition is overlooked by the examiner at the autopsy, for unless his attention has been called to the possible occurrence of such an anomaly it is easily missed in a careless or hasty examination; the usual manner of removing the heart is of itself disadvantageous, for the knife frequently severs the great vessels at or near the point at which the duct connects them.

Such cases, tabulated as above according to sex and to the age at which death occurred, show two interesting facts: (1) A decided preponderance of females, for which no explanation seems to have been offered; and (2) that the presence of this lesion is by no means incompatible with a fair duration of life, although perhaps shortening it, since few of the subjects passed the fiftieth year. As in my own case, the patient may live an active and vigorous life although his duct is patent enough to cause marked physical findings, and death occurs from some unrelated affection.

**THE NORMAL OCCLUSION AND OBLITERATION OF THE DUCTUS ARTERIOSUS.** In order to understand the reasons for the occasional failure of the ductus arteriosus to undergo normal occlusion and involution, it is necessary to become familiar with the mechanism

by which this process is normally accomplished. There have been many hypotheses advanced to explain how and why the duct becomes spontaneously occluded, synchronously with the first successful efforts of the newborn babe to breathe. Among them may be mentioned the following: That the first expansion of the large bronchi by air compresses the duct (King); thrombosis and adhesion of the walls (Cruveilhier, and others); bending of the arch of the aorta by the increased pressure after birth (Magendie); tension and collapse through change of position of the thoracic viscera upon the beginning of respiration (Schantz,<sup>10</sup> Gérard); occlusion by fibrous growth in the intima (Thoma, Walkoff); active contraction by the muscular layers of the wall of the duct (Billard, Langer). I may mention particularly the suggestion of W. S. Forbes,<sup>11</sup> of Philadelphia (1880), that fibrous bands which pass over the duct are connected with the diaphragm, and upon its first descent are pulled down upon the duct and occlude it. However plausible some of these explanations may be, it is quite certain that not all of them apply to the normal process of closure of the duct. This is a physiological process taking place spontaneously and instantaneously in every newborn child, and therefore there must be some mechanism which can be relied upon always to perform this occlusion. Any explanation which involves connective tissue proliferation must be inadequate, for the duct is patent and carrying on its full function up to the moment of delivery, and then is at once occluded when the child begins to breathe; it is necessary to distinguish between the instantaneous *occlusion* of the duct and its subsequent *obliteration*. The theory of occlusion by thrombosis is also faulty, for ordinarily the occluded duct does not contain thrombi; even the ultimate obliteration is accomplished without the participation of thrombi, by means of the proliferation of the intimal connective tissue. All the hypotheses that are based upon the intermittent pressure from the respiratory act are obliged to assume the formation of thrombi to account for the permanence of the occlusion, since intermittent respiratory motions would only produce an intermittent form of occlusion, and hence these views must all be incorrect. What seems to be the proper explanation is the outcome of the investigations begun by Zuntz and carried on by Strassmann. Zuntz observed that at the aortic opening of the duct in full term animals there is present a thin crescentic fold along the upper margin, which is formed through the manner of insertion of the duct into the aorta; this insertion is at an extremely acute angle, about 33 degrees, so that the margin is thinned out to form the fold. This observation was extended by Strassmann to fetuses of various species, including human, and investigated experimentally and microscopically. Zweifel corrob-

<sup>10</sup> Pfüger's Archiv, 1889, xliv, 239.

<sup>11</sup> AMER. JOUR. MED. SCI., 1880, lxxx, 88.

rated the correctness of these findings in the human foetus, and the work has received further support from Roeder.<sup>12</sup>

In the human embryo the first signs of this fold begin to appear at about the sixth month, but it is not fully developed until the end of the eighth month, which possibly accounts for the failure of some apparently viable premature infants to live. The mechanism by which the fold at the aortic end of the duct accomplishes occlusion is as follows: In the foetus *in utero* the pressure in the pulmonary artery is considerably greater than in the aorta, probably as high as a ratio of three to one; consequently blood flows through the duct (at this time larger than either of the two main divisions of the pulmonary artery) into the aorta. As soon as respiration begins, however, the dilatation of the lungs relieves the obstruction to the pulmonary vessels, more blood enters the left heart from the pulmonary veins, and consequently the pressure in the pulmonary artery falls and the aortic pressure rises, so that the relation of pressure becomes as much higher in favor of the aorta as it formerly was in favor of the pulmonary artery. As a result, blood ceases to pass from the pulmonary artery through the ductus arteriosus toward the aorta, and it cannot pass in the other direction because the pressure within the aorta forces the thin elongated margin against the opposite wall of the duct, blocking it completely. Strassmann tested the competency of this mechanism, and found that in the fully developed foetus fluid injected into the pulmonary artery at pressures corresponding to the normal will pass readily through the duct into the aorta, but fluids injected into the aorta at normal pressure do not enter the pulmonary artery at all. If the pressure is considerably raised above the normal, the flap at the orifice of the duct becomes incompetent, either through its own stretching or through dilatation of the orifice, and extreme pressure may invert the flap into the duct.

It is in this way that the remarkable immediate occlusion of the duct at birth is accomplished. As long as the occlusion exists the duct has no function, and it at once begins to undergo changes of involution similar to those described by Thoma in the hypogastric arteries at the same period of life, or in ligated vessels between the ligature and the nearest branch. Apparently the contractility of the wall of the duct, although it is relatively poor in both elastic and muscular elements, is sufficient to prevent the entrance of blood from the pulmonary artery after the pressure in that vessel falls, for the finding of thrombi in the occluded duct is very exceptional. Different investigators disagree as to the point at which obliteration is first complete, some stating that the narrowed central portion is first completely occluded by the growth and contraction of the subintimal

<sup>12</sup> Gérard does not seem to have been able to confirm Strassmann's work, but his statements on this point are not extensive enough to assure one that his criticism is valuable.

connective tissue, while others maintain that obliteration takes place first at the ends of the duct. These differences concerning a simple matter of fact probably mean that there is no regularity in the place at which obliteration does first occur.

In the course of time fibrous tissue replaces the muscular and elastic tissues, so that these elements are scanty or wanting in the fibrous ligamentum arteriosus of the adult. Occasionally, however, remains of the original endothelial-lined canal can be found microscopically; and not infrequently the duct remains permeable to a fine probe for a few millimeters, most often at the pulmonary end. The length of the duct is, of course, modified by these changes; during the first two or three weeks it lengthens slightly, with the development of the thoracic organs, then gradually decreases a few millimeters in the child, but in the adult the ligamentum arteriosus is fully as long as the original duct, and often much longer. However, the length of the ligament is a very variable quantity, sometimes reaching 20 mm., and sometimes being practically absent, the aorta and pulmonary artery being then intimately adherent at this point.

**ETIOLOGY OF PERSISTENT PATENCY.** With the above facts in mind concerning the mechanism of normal occlusion of the ductus arteriosus, the conditions leading to persistent patency may be readily understood. Virchow considered these cases as of two classes: *primary patency*, in which occlusion of the duct had never occurred; and *secondary*, in which the duct reopened after having been more or less perfectly closed. The French writers consider as primary those cases in which the patency of the duct is the sole cardiovascular anomaly, and call the more common condition, in which there are other developmental defects in the heart and great vessels, *secondary patency*. It is possible to imagine that the duct may fail to become occluded, because of any one of the following causes:

1. When the insertion of the duct into the aorta forms a less acute angle than normal, the conditions necessary for the formation and functionation of the membranous fold of Zuntz and Strassmann at the aortic orifice of the duct are not present.

2. Local conditions, such as intra-uterine aortitis, congenital syphilis, or inadequate growth energy, may prevent the proper formation of the occlusive fold. Rickets has been present quite frequently in this condition.

3. Premature birth, as the fold is not completely developed until the end of the eighth month. Cases in which premature birth seems to have been the cause of subsequent patency have been reported by Bittorf,<sup>13</sup> whose patient was alive at twelve years, and by Rees<sup>14</sup> and Dresler.<sup>15</sup>

<sup>13</sup> Münch. med. Woch., 1903, 1, 1771.

<sup>14</sup> Trans. London Pathol. Society, 1848, i, 203.

<sup>15</sup> Jahrb. f. Kinderheilk., 1902, lvi, 705.

4. An abnormally large lumen or aortic orifice of the duct might render the fold inadequate.

5. Persistent high pressure in the pulmonary circulation, such as might be produced by respiratory difficulties in the newborn, or stenosis of the pulmonary arteries beyond the duct. Atelectasis is especially important in this connection, as also is acute bronchitis; and in a case of Roeder's a congenital goitre pressed upon the trachea.

6. Relatively low pressure in the aorta, as in congenital stenosis of the aorta or the aortic orifice of the left ventricle, in which case the duct is always patent and circulation is carried on as in the foetus, by means of the pulmonary artery and the duct.

7. Excessive pressure in the aorta at or immediately after birth, by rendering the occlusive fold at the aortic end of the duct either relatively or absolutely incompetent.

Secondary patency, through reopening of an already occluded duct, is probably a relatively uncommon occurrence; yet it can be imagined that it might be produced in one of the following ways:

1. If shortly after birth, before obliterative changes have rendered the duct impermeable, the pulmonic blood pressure is unduly raised by respiratory troubles, such as bronchitis, atelectasis, pleural effusions, etc., blood may be forced through the duct toward the aorta under some considerable pressure; at this time the walls of the duct are considerably weakened by the degenerative changes that are associated with the obliterative process, so that they may readily become dilated and render the duct permanently patent. Roeder found that although the duct of the newly born foetus will withstand a pressure of 80 mm. of mercury, which is above the normal pulmonic pressure of the foetus, at 90. mm. aneurysmal dilatation begins, and at 110 to 120 mm. serious dilatation and damage to the media occurs. He believes that such pressures may be reached when the child is under the pressure of the expulsive forces of labor, and that if there is in the first few days any respiratory difficulty that causes blood to pass into the duct from the pulmonary artery, then dilatation and patency may become permanent, or, as in two of his cases, rupture may occur. It would seem probable that similar conditions may result in the thrombosed dilatation, aneurysms of the ductus arteriosus, which are observed not infrequently in young infants, and described by Gérard, Roeder, and others.

2. In cases of septic infection of the newborn, at the umbilicus or elsewhere, the obliterating duct is a favorable site for the formation of septic thrombi, which may prevent the normal obliterative processes and render the duct patent. Although Lancereaux and Rauchfuss believed that this is a common cause of patency, it is probable that such septic thrombosis is usually fatal, and therefore it can have little to do with persistence of the duct in the adult. Nevertheless, it is of interest to note that thrombosis of the ductus arteriosus, if present at all, is usually associated with septic processes.

3. It is quite possible that the fibrous obliteration of the ductus may be faulty even after proper temporary occlusion has occurred; as the child develops and blood pressure increases, the sclerotic ring at the aortic orifice of such an imperfectly occluded canal may dilate under the pressure of the blood, which then gradually forces open the old canal. Those cases in which the pulmonary end of the patent duct is more or less occluded by a perforated membrane, as in the cases described by Rokitsansky, Wagener and in my own case, may be explained as due to a gradual reopening of an imperfectly obliterated ductus until the closed pulmonic end has been forced out into the pulmonary artery and ruptured.

When we take into account all the ways in which pathological patency might possibly be produced, the fact that such patency is one of the most infrequent of pathological rarities is striking, and shows that under almost any condition the methods of closure are adequate. Probably the chief reserve defence, or "factor of safety," lies in the sclerotic obliteration of the duct, which may well be adequate to accomplish secondary occlusion even if the primary occlusion at the aortic orifice is defective. It is also possible, however, that failure of closure of the duct is a more common cause of unexpected death of newborn infants than is realized. Roeder suggests that in infants with respiratory difficulties may frequently die because of reopening of the duct on account of the heightened pulmonary blood pressure, the mixing of the aortic and pulmonic currents that then occurs being incompatible with their existence.

If we look through the records of the cases that have been reported, it is apparent that, at least in infants, respiratory disturbances with the resulting rise in pulmonary blood pressure is a most important factor in all forms of ductus arteriosus defects, including not only patency, but also thrombosis, aneurysm, and rupture. In most of the adult patients, however, it has been impossible to ascribe a cause, probably because the infantile history is not known. Congenital syphilis does not seem to have been present, although it could be easily understood how it might influence the production of the anomaly. Many of the patients have been small, rachitic, and poorly developed, as if the developmental forces had been defective, but it is possible that the poor development may have been the result rather than the cause of the arterial anomaly. Heredity seems to play an important part in all forms of congenital heart disease, and it may be concerned in this particular form of circulatory malformation, as shown by the remarkable family studied by de la Camp.<sup>16</sup> In this family of six children all showed clinical evidence of having persistence of the ductus arteriosus; in the two oldest children, sisters, the manifestations were very pronounced and the lesions were causing circulatory embarrassment, while in the younger children the results had not

<sup>16</sup> Berl. klin. Woch., 1903, xl, 48.



become so evident. Although in none of these cases has anatomical proof of the diagnosis been secured, yet the clinical findings and the radiograms are sufficiently characteristic to make the diagnosis reasonably positive, at least in the more advanced cases. The parents of the children are both living and free from any signs of cardiac disturbance.

In a few cases there have been observed other developmental defects, suggesting that the arterial abnormality might be due to defective developmental forces. In one case hypospadias was present, in the case of Bittorf there was double inguinal hernia, and in my own case here was a short inguinal hernia. However, developmental defects have been observed so infrequently that they are probably of little significance. In a very considerable number of the cases a history of alcoholism in the father has been obtained, but it is rather difficult to establish a relation between this and the patency of the duct in the offspring.

**PATHOLOGICAL ANATOMY.** Gérard classifies the conditions under which patency of the ductus arteriosus may occur as follows:

I. Simple, uncomplicated persistence of the ductus arteriosus.

II. Accompanied by malformations of the vessels, as follows:

(A) Permanence of orifices that are normally closed (before), at or after the moment of birth (arrest of development or malformations).

(a) Interventricular communication.

(b) Stenosis of the pulmonary artery either at its origin or in its course.

(c) Absence of the pulmonary artery.

(d) Anomalies in the aorta.

(B) Persistence of the foramen ovale.

(C) Multiple malformations, which affect all the anatomy and are incompatible with life.

III. Accompanied by malformations in more remote places (hypospadias, hernias, etc.) or by superimposed lesions (atheroma, acute aortitis).

In his classical article upon this subject Gerhardt divided the forms assumed by the duct itself into four groups, as follows:

1. Extreme shortening of the canal, so that it forms little more than the margin of the opening in both vessels.

2. Funnel shaped, with the wide end toward the aorta.

3. Cylindrical form, the duct being variable in length and width.

4. Aneurysmal dilatations of the canal.

Of these forms, by far the most common are the second and third types, in which there is a definite duct. Even in the cylindrical type the aortic orifice is generally larger than the pulmonary opening, and so there is more or less approximation to the funnel shape. My own case is an excellent example of this, the elliptical aortic orifice measuring 8 x 6 mm., the duct maintaining nearly the same diameter

until near the pulmonary opening, where it narrows abruptly. In all the cases in adults there is usually considerable sclerosis of the aorta just about the orifice of the duct, and also in the walls of the duct itself, which last feature is particularly marked in my own case. Presumably the sclerosis of the aorta depends upon the traction of the duct (Thoma); indeed, in normal individuals one of the first places in which a sclerotic patch appears in the aorta is usually just at the point of insertion of the arterial ligament. Thoma has suggested that some of these cases of funnel-shaped patent ducts are really examples of traction diverticula of the aorta, but this is probably incorrect, for, as Wagener points out, if the arterial ligament were exerting traction one would expect that the thin-walled pulmonary artery would give way rather than the more rigid aorta. In my case there was a small traction diverticulum of the oesophagus, and although no adherent tissue was demonstrable at the autopsy, it seems quite possible that the existence of the patent duct may have in some way caused this diverticulum.

The length of the patent duct in the adult cases is extremely variable, from practically nothing at all, in the first of Gerhardt's groups, to as much as 20 mm.; but generally it is shorter than the 16 mm. duct found present in my case. The diameter of the lumen is usually from 3 to 6 mm., but there are cases of dilatation to 1 cm. or even more; in two cases the duct permitted the entrance of the little finger, and Sanders (1860) described the lumen in his case as being as large as the descending aorta of the infant in which it was found.

On account of the eddying of conflicting currents at the point of entrance of the duct into the pulmonary artery, formation of thrombotic vegetations at this point is favored, and in cases of septic conditions or acute endarteritis, vegetations may form in and about the openings of a patent duct; such a case is illustrated in the article by Hochhaus.<sup>17</sup> Schlagenhauser<sup>18</sup> has described an interesting case of acute aortic endocarditis produced by the influenza bacillus in a patient with a patent ductus arteriosus; vegetations were also present extending through the lumen of the duct and at both orifices, and from these pulmonary infarcts had been produced. I have already mentioned the fact that thrombosis may occur in the duct of newborn children with septic infections, especially of the umbilical cord; Rauchfuss observed this condition twelve times in 1400 autopsies on infants, in 2 of which the thrombi were purulent. Roeder's 2 cases, in which partial rupture of the duct was present in children aged, respectively, two and three days, are unique.

Two features that were present in some of the recorded cases have particular interest in connection with the pathogenesis of persistent patency, and they have been discussed and described particularly by Wagener, whose two cases presented these features. They are

<sup>17</sup> Deut. Arch. klin. Med., 1892, II, 1.

<sup>18</sup> Ztschr. f. Heilk., 1901, xxii, 19.

(1) a fold guarding the aortic end of the duct, and (2) the mound-like elevation upon which the pulmonic end opens. There can be little question that the fold across the aortic opening represents the membranous margin, described by Zuntz and Strassmann, which under normal conditions closes the entrance to the duct from the aorta. Normally this fold becomes fused with the surface of the duct against which it is forced by the aortic pressure, and loses its identity during the subsequent processes of sclerosis. In case it does not occlude the duct for any reason, it might well remain as a fold or ridge at the entrance to the duct; such a fold has been described in several cases.

The protrusion of the margins of the pulmonary orifice has been described in a number of cases, and is particularly well shown in my own case (Fig. 2). Rokitsansky, indeed, says that the pulmonary orifice is always a small round ostium, which is surrounded by a wall and is located on the top of a papilla that seems to have been formed by the pushing out or evagination of the end of the duct. In Wagener's three cases there was a delicate membrane separating the lumen of the duct from the lumen of the pulmonary artery, into which this membrane protruded; in two of the cases the membrane occluded the duct entirely, and in one there were small perforations. The significance of this membrane or elevation at the pulmonary ostium of the duct is of interest, but it has not been determined. Gerhardt looked upon the membrane as the remains of an organized thrombus, but there is no good evidence to support this idea. It seems much more probable that it represents a tissue formed in the closure of the duct at the pulmonary end, which has later been forced into the pulmonary artery by the aortic pressure after the duct has been gradually dilated from the unclosed aortic end. Another possibility, also, is that the elevation represents the result of an inflammatory proliferation set up at the point where the aortic and pulmonic currents meet; in favor of this view are the histological findings in Wagener's cases, which were interpreted by this author as indicating a recently formed tissue. If the first manner of formation occurs, then we may have signs of patent ductus arteriosus appearing for the first time in adult life, through the opening up of an imperfectly occluded duct; on the other hand, if the proliferation reaction occurs at the pulmonary ostium, it is possible that the signs of patency may disappear because of spontaneous closure at this point, and there is at least one authentic instance of recovery from this condition (Balfour)<sup>19</sup> to support the latter hypothesis.

Aneurysmal dilatations have been observed chiefly in infants, usually associated with thrombosis. Gérard (1903) collected 17 cases from the literature, but he apparently examined only French

<sup>19</sup> "Clinical Lectures on Diseases of the Heart and Aorta," 1898, 3d edition, p. 243.

publications, for there have been many others published in other languages. In 1000 autopsies on children Thore (1850) found 8 instances of this condition, and Gérard found 2 in 100 infant cadavers, so that it is not an extremely unusual condition. The aneurysms undergo thrombotic occlusion early, being always found in this condition at autopsy, so that the reason they are not found in adults is probably that they are obliterated by connective tissue formation. The shape is usually spherical, and the size "from a coffee bean to a hazel-nut." The location is usually nearer the pulmonic than the aortic end. Since in all these cases the duct is occluded by thrombosis, they do not properly come into consideration as examples of patent ductus arteriosus. In one of Roeder's cases of rupture of the duct there was present a form of dissecting aneurysm. He thinks that high blood pressure during delivery may injure the duct and lead to aneurysm later if the duct remains patent, or, in other cases, that blood entering the weakened duct from the pulmonary artery after changes of involution have begun causes the aneurysmal dilatation. Since the duct is occluded by thrombosis, aneurysm is not incompatible with life, and is merely an autopsy finding. Some of the more dilated of the patent ducts found in adult cases may be looked upon as a form of aneurysm, but I have found no records of extensive, typical, aneurysmal dilatation, with its usual extension and pressure effects.

**RESULTS OF PATENCY OF THE DUCTUS ARTERIOSUS.** These are very difficult to estimate, for the reports to be found in the literature give extremely varying pictures. In some cases a well-opened duct has been found in the body of an adult, without subjective signs or objective symptoms having been noticed during life, while, on the other hand, some writers believe that in infants failure of the duct to close is in many instances incompatible with life, the blood which enters the pulmonary artery under aortic pressure either interfering with the pulmonary circulation or else causing respiratory troubles. Obviously the results will depend largely upon the degree of patency that exists, and in such cases as those of Wagener, in which only minute perforations through an occluding membrane are present, it is certain that no ill effects could be produced. Very commonly, as in my case, the opening is large enough to lead to the presence of symptoms and signs of the lesion, yet without sufficient disturbance of the circulation resulting to interfere seriously with the health and activities of the patient. The great majority of the cases observed clinically and at autopsy are of this nature, and in very few of the latter cases has death been due to cardiac insufficiency. However, there are a few instances in which the communication between the pulmonic and the aortic circulation has been so free that serious disturbances have resulted. In some cases death has occurred in infancy with all the usual manifestations of a serious anomaly of the circulatory system; in a greater number

of cases the patient has suffered from childhood with palpitation, shortness of breath, and inability to perform severe or continued muscular exertion, these symptoms either continuing until the patient succumbs to some intercurrent affection, or, more rarely, dies from cardiac incompetence and its results. In the more typical cases cyanosis is either slight or entirely absent, for here the amount of blood going to the lungs is larger than normal, in contrast to the more common condition of pulmonary stenosis. Even in the simplest cases the heart is usually more or less affected. Almost always there is some degree of hypertrophy of the right ventricle, and frequently dilatation, because of the obstruction to the emptying of the right ventricle caused by the intrushing arterial current. As there is more blood passing through the pulmonary circuit than normal, the left auricle is usually dilated, and hypertrophy of the left ventricle may result from moving this increased volume of blood and in keeping up the aortic pressure. The pulmonary artery is dilated by the pressure, and in some cases sclerosis occurs. Von Schrötter has reported a case in which the dilated duct produced pressure upon the left recurrent laryngeal nerve, which passes about the aorta in immediate proximity to the duct. The foramen ovale is frequently found incompletely closed, but this is so common an occurrence, even in normal individuals, that it can only be considered when the foramen is not guarded, in the usual way, by the slit-like nature of the opening, but is functionally patent; but in this case we should be dealing with one of the more common conditions of multiple congenital circulatory anomalies, and not the simple or primary patency of the duct with which we are concerned.

**DIAGNOSIS.** Although there are a few writers who, like Gérard, question the possibility of a positive clinical diagnosis of simple patency of the ductus arteriosus being made, yet there are certainly abundant clinical reports in which this diagnosis has been made with some degree of assurance, and in a few instances the antemortem diagnosis has been substantiated by postmortem demonstration. Quite a number of German clinicians have reported cases of patent ductus arteriosus based solely upon the clinical findings, and the supposedly characteristic features are brought out in their publications, among which may be mentioned, as among the more recent and instructive, those of Zinn,<sup>19</sup> de la Camp, Dresler, Arnheim,<sup>20</sup> Heichelheim,<sup>21</sup> Brettauer,<sup>22</sup> Schiffer,<sup>23</sup> Sidlauer<sup>24</sup> and Bittorf. Dalsjö,<sup>25</sup> in Sweden, has also described two interesting clinical cases

<sup>19</sup> Berl. klin. Woch., 1898, xxxv, 433 and 850.

<sup>20</sup> Ibid., 1903, xl, 616.

<sup>21</sup> Deut. med. Woch., 1903, xxix, 280 (Vereins Beilage).

<sup>22</sup> "Drei Fälle Persistens des Ductus Arteriosus Botalli," Zurich, 1905. W. Conradi-Maag.

<sup>23</sup> "Kasualistische Beiträge zur klinischen Diagnostik der Persistenz des Ductus Arteriosus Botalli" (Giessen), Würzburg, 1903. H. Stürtz.

<sup>24</sup> Arch. f. Kinderheilk., 1902, xxxiv, 331.

<sup>25</sup> Hygiea, Stockholm, 1904, iv, 225.

Perhaps the most positive in his opinion concerning the possibility of accurate diagnosis of this condition is G. A. Gibson,<sup>22</sup> of Edinburgh, who is fortified in this by the corroboration at postmortem of his diagnosis in one of his several clinical cases. Concerning the chief diagnostic characteristics, he makes the following statement: "Inspection may reveal no facts of importance; palpation yields the valuable sign of a long thrill following the apical impulse, and continuing beyond the recoil of the blood on the semilunar cusps, the shock of which may be felt during the thrill; percussion may negative the suspicion of any increase in cardiac dullness—in fact, it usually does so in uncomplicated cases; auscultation gives the second and the most invariable evidence of the lesion in the presence of a murmur which is pathognomonic. Beginning distinctly after the first sound, it accompanies the latter part of that sound, occupies the first pause, accompanies the second sound, which may be accentuated in the pulmonary area or may be doubled, and finally dies away during the long pause." Besides these features, the German clinical observers lay much stress upon a band-like area of dullness along the left margin of the sternum in the second and third intercostal spaces, produced by the dilatation of the pulmonary artery, and over which the murmur and thrill are most distinct; this feature was first emphasized by Gerhardt. The murmur is also quite distinct in the upper part of the left interscapular space (François-Franck). The dilatation of the pulmonary artery can be readily observed in radiograms, the shadow above the base of the heart pulsating synchronously with each ventricular systole; this feature is emphasized by all the more recent observers; generally the auricles and right ventricle are also enlarged. De la Camp insists upon the significance of the direction of the thrill, which can be palpated readily in the second and third left intercostal spaces when the opening is not too small; the thrill seems to travel from below out and to the left, upward, inward, and to the right; when this feature can be made out it is pathognomonic. Generally the murmur is transmitted into the carotids, and in many cases it is heard more loudly in the left than in the right; in several cases the left radial pulse has not been so strong as the right, although this is by no means characteristic. It should also be mentioned, in contradiction to Gibson's statement, that hypertrophy or dilatation of the heart to greater or less degree has been present in by far the larger number of all cases observed, whether clinically or at autopsy. In differentiation from the other congenital cardiac lesions, especially stenosis of the pulmonary artery, which is the most common, the absence or relatively slight amount of cyanosis is quite characteristic of patency of the ductus arteriosus. The sharp closure of the pulmonary valves, which is emphasized by several writers, is not always present,

<sup>22</sup> Med. Press and Circular, 1906, lxxxi, 572; Edinburgh Med. Jour., 1900, viii, n. s., 1.

possibly because when the pulmonary pressure becomes very considerably raised the cusps do not open wide enough to close sharply. In some cases there has been observed a form of *pulsus paradoxus*, four or five beats of full strength being followed by a similar number of weaker beats; this phenomenon is explained by François-Franck as due to a more rapid escape of blood from the aorta into the pulmonary artery during inspiration—which lowers the aortic pressure and weakens the pulse during this period.

From what can be learned in the latest writings it would seem that a positive diagnosis should be possible in typical cases, but there are many cases reported in which the clinical findings have been anything but typical. It must also be admitted that a small aneurysm of the aorta communicating with the pulmonary artery might produce the same effects, as shown by Brocq's<sup>27</sup> case, although it would probably appear suddenly and later in life than the congenital vascular abnormality. Particular emphasis is laid upon the importance of accurate diagnosis of this condition by the bold suggestion [of Munro,<sup>28</sup> that it should be possible to close this abnormal channel by surgical intervention. He has convinced himself by operations upon the cadaver that such operative procedure is possible, the duct being reached by an incision dividing the sternum or cutting through the attachment of the ribs on the left side; its closure could be accomplished by ligature, or perhaps by crushing. Whether a patient with the poor condition of circulation and respiration which most of these patients exhibit in any case serious enough to warrant such a dangerous intervention could stand so severe an operation, is a question that would have to be decided for each individual case; it must also be considered whether the weakened circulatory apparatus would not be seriously embarrassed by the sudden stopping of a condition to which it has adapted itself to a greater or less degree. In any case, however, this suggestion is well worthy of consideration, and it does not seem so fantastic and impossible as it would have a few years ago, before successful operations upon the heart became a not uncommon occurrence.

Another reason for establishing an accurate diagnosis in these cases is that the prognosis is, as a general thing, better than in other congenital heart lesions. Cyanosis, congestion, and cedema are present only in exceptionally severe cases, in which the opening has been unusually large and when the patient has reached the last stages. The advanced age at which several of these patients have died and the absence or unimportance of the symptoms resulting from the lesions in most of the recorded cases are noticeable features. It is also perfectly possible for healing to occur; this might either be brought about through thrombosis, or, as appears to be shown in my own case, a reactive proliferation at the margins of the opening

<sup>27</sup> *Rev. de méd.*, 1885, v, 1046; 1886, vi, 786.

<sup>28</sup> *Annals of Surgery*, 1907, xlv, 335.

of the duct into the pulmonary artery may cause occlusion of or at least an amelioration of the condition. Balfour has described what seems to be an instance of such spontaneous recovery. The patient was, in childhood, examined by James Begbie, who made a diagnosis of patent ductus arteriosus; ten years later the same diagnosis was made by Warburton Begbie, and ten years later by Balfour, the same diagnosis having also been made in the interim by Sanders. The patient was frequently observed from this time on by Balfour, and the condition gradually improved, until fifteen years after Balfour's first examination the lesion seemed to have become entirely healed.

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### LEUKANEMIA.

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THE symptom complex first described by von Leube under the name of leukanemia has been a subject for discussion for several years; certain authors contend that it is only an atypical form of pseudoleukemia or leukemia, while others claim it to be a clinical entity, a true combination of leukemia and pernicious anemia. The following case resembles so closely those described by von Leube and others, that it seems worthy of discussion:

Mrs. J., aged twenty-five years, a Syrian, married, and a housewife, entered the Rebekah Hospital, April 22, 1907, complaining of weakness, dizziness, tinnitus aurium, extreme nervousness, and constipation. Her father, mother, and three sisters are in good health. There is no history of tuberculosis, insanity, or malignant disease in the family. The patient was rather delicate as a child; had measles when one year old, and smallpox when twelve years old. The menstrual history is without interest. She married at eighteen years of age; has three children, all in good health. She had a small abscess of the left breast after the birth of the first child; this healed without complications. The last child was born eleven months ago.

The patient came to America three years ago in perfect health, and remained so until March 10, 1907, when she had an attack of grip lasting about a week, at the end of which time she was able to attend to her household duties, although still somewhat weak. A week later a friend commented on her palor. About March 22 she began to notice increasing weakness and slight dyspnoea after climbing stairs or other exertion. On March 28 she was severely frightened by an insane person, and from that time on weakness developed rapidly. By April 10 weakness had become so marked



that she had difficulty in going about her work. Shortly after this she came to St. Louis and consulted a physician. Roaring noises in the head and weakness were at this time her only complaints. Weakness became more and more pronounced, sleep disturbed, and she began to be very nervous. She had never noticed any enlargement in the abdomen until this was pointed out by her physician just before entering the hospital. She eats and sleeps regularly, and uses no alcohol or drugs.

*Physical Examination.* April 25. Fairly well nourished woman; five feet two inches in height; weight, 110 pounds. (Normal weight, 120.) Temperature, 101°; pulse, 120, soft and bounding. The skin of head and face is pale and of a yellowish brown color, due in part to the natural swarthy complexion of her race. Many deep scars (smallpox) appear paler than the surrounding skin. The ears are very pale; there is no discharge; the hearing is acute. The eyes are rather dull, the conjunctivæ of a dirty yellowish tint.

The lips are very pale and dry. The mucous membrane of mouth is very pale; no ulcerations or abrasions. The tonsils are slightly enlarged and pale; no exudate. There are no enlarged glands in the neck or the axilla. Physical examination of the lungs shows no deviation from the normal. The apex impulse is plainly seen in the fifth intercostal space four inches from the midsternal line; it is rather quick and slapping in character. The absolute heart dulness begins at the fourth intercostal space and extends to the sixth rib in the parasternal line and four inches to the left of the midsternal line in the fifth intercostal space. At the apex the first sound of the heart is short and valvular in character; the second sound is rather loud and clear; at the aortic area both sounds are fairly clear and distinct; at the pulmonic area a blowing systolic murmur is heard and is transmitted in all directions for about two inches; the second sound is clear, but not accentuated. The liver dulness begins at the sixth rib in the parasternal line and extends two inches below the costal margin; at the midaxillary line it begins at the eighth rib and extends to the costal margin. The liver can be plainly felt two inches below the costal margin; hard, smooth, and not sensitive to pressure. The splenic dulness begins at the eighth rib in the midscapular line. The spleen extends from the margin of the ribs to the crest of the ilium and to the right as far as the navel; it is smooth, not sensitive to pressure. It causes prominence of the whole left abdomen. A notch can be felt at the level of the navel. There is slight tenderness in the right ovarian region. The genital organs are apparently normal, except for slight peroneal tear. There are no enlarged inguinal or popliteal glands, but there is very slight oedema at both ankles.

Urine (24-hour specimen): Quantity, 1050 c.c.; specific gravity 1014; no albumin or sugar; trace of albumoses. Sediment shows many epithelial cells, but no casts or leukocytes.

Feces: Hard; dark-brownish in color; very offensive odor; few particles of undigested food noticed. Microscopic examination reveals no animal parasites.

Blood examination (for details of the various counts see table): Remarkably low count of red cells; moderate increase of white cells, with slight relative increase of lymphocytes, and a small percentage of myelocytes; total absence of mast cells at all times. Especially noteworthy, is the remarkable number of young forms, both normoblasts and megaloblasts, often as many as five or six in each microscopic field. The megaloblastic forms show the greatest variation in size and shape. The nuclei are often of peculiar shape; multiple nuclei are not uncommon. They have a somewhat reticulated texture which stains rather poorly. Polychromatophilia is the rule with these forms. I am not prepared to state whether the lobulated or multinuclear forms are simply degeneration forms, or reversions to an early embryonic type, but the former explanation seems the more plausible.

On subsequent examinations the number of nucleated forms varied considerably in numbers, but the types illustrated could be found in almost every blood film examined from April 23 to the time of the patient's death.

Date.	Number red blood cells per c.mm.	Hemoglobin.	Number white blood cells per c.mm.	Small lymphocytes.	Large lymphocytes.	Polynuclear leukocytes.	Eosinophile mononuclear leukocytes.	Eosinophile polynuclear leukocytes.	Myelocytes.	Mast cells.	Number of normoblasts seen in counting 500 white cells.	Number of megaloblasts seen in counting 500 white cells.
		%		%	%	%	%	%	%	%		
April 23	850,000	30	16,000	21	6.2	62.5	..	2.5	5.0	..	80	120
April 28	800,000	30	14,000	31	6.8	55.2	0.6	1.0	5.4	..	95	140
May 5	880,000	35	17,000	27	6.0	59.0	..	2.0	6.0	..	70	100
May 12	900,000	35	18,200	20	5.2	63.0	..	3.6	8.0	..	65	48
May 18	800,000	30	17,061	23	7.2	57.0	1.6	2.2	9.0	..	70	90
May 24	700,000	20	12,000	30	8.0	48.0	2.0	1.0	11.0	..	22	12

During the first week of the patient's stay in the hospital, weakness continued to be her most distressing symptom; the temperature ranged from 101° to 102.3°, the pulse from 120 to 130. The bowels were kept regular with 5-grain doses of phenolphthalein daily. Fowler's solution in 5-drop doses was given after meals, increasing the amount by 1 drop every other day. The urine and stools remained practically negative.

On April 28 the patient began to complain of slight pain in the

right ear, but examination proved negative. By the end of the first week she began to show slight improvement; the temperature ranged from 99° to 100.5°. The appetite improved somewhat; sleep was not so restless. The bowels, however, did not move so freely, and a soap enema was ordered, followed by a pill of aloin, belladonna, and strychnine to replace the phenolphthalein. Pain in the right ear became more severe. Examination revealed slight redness of the posterior portion of the external canal, and the drum head slightly cloudy but not bulging.

During the second week the patient's general condition improved steadily; the temperature ranged from 98.2° to 99.6°, the pulse from 110 to 120; the appetite remained fairly good, and the bowels regular. The patient slept a great deal. Roaring noises in the head were still annoying and pain in the ear had not improved. Examination showed increased redness of the external canal, and the drum head seemed to be slightly bulging. The spleen and liver showed no appreciable change. The heart action was very rapid, but regular; the hemic murmur in the pulmonic region persisted.

On May 8 the patient noticed during the previous night slight discharge from the right ear followed by considerable relief. Examination showed a small rent in the drum head, which was covered with thick yellow pus, from which cultures were made. The ear was irrigated with boric acid and adrenalin solution.

On May 15 the patient felt a little stronger; the temperature during the previous week reached 100° only once. The appetite was good; she sleeps a great deal. The discharge from ear had almost ceased. Cultures showed streptococcus and various other organisms (probably due to contamination).

On May 18 the patient complained of increasing weakness in the last few days; nervousness had also increased markedly; roaring noises in the head had become somewhat more annoying; temperature was not above 99°; the pulse, however, remained between 110 and 120. Physical examination showed little change from the day of admission. The urine still contained traces of albumoses. The stools remained negative except for evidences of intestinal indigestion. At this time the patient was taking 15 drops of Fowler's solution after meals. She refused to stay longer in the hospital.

On May 26 I was called to patient's house. She was very weak; pulse, 130; respiration, 36 and sighing in character. Physical examination showed no change in the liver or spleen. The heart dulness was slightly increased and the sounds were very weak. The murmur in the pulmonic area had almost disappeared.

On May 28 the patient died. An autopsy could not be obtained.

The general symptoms in this case resemble quite closely those of pernicious anemia, while the physical signs might be taken as almost positive evidence of splenic or splenomyelogenous leukemia.

The blood picture, however, is most unusual; while in the main it resembles pernicious anemia and myelogenous leukemia, the number of young forms is much greater than is found in either leukemia or pernicious anemia. One must consider the relatively small number of cells present, making the number of nucleated forms relatively more numerous. The otitis media may have had some bearing on the case, as many authors have noted streptococcic infections complicating leukemias, or followed by a leukemic blood-picture. The late appearance and the fact that the existing blood-picture was not appreciably modified by it would, I think, indicate that it was only incidental and had no important bearing on the progress of the disease.

The case described by von Leube<sup>1</sup> was that of a boy, aged ten years, who was brought to the hospital unconscious. Three days previous his teacher had noticed that he was very pale, and two days later he began to complain of pain in the neck and nose bleed and became unconscious. Physical examination showed the temperature 101°; the pupils equal; no stiffness in the neck; the skin and mucous membranes very pale; liver and spleen greatly enlarged; the heart dullness increased, but no murmurs. Blood examination: red cells, 256,000; white cells, 10,500; hemoglobin, 10 per cent.; nucleated red cells very numerous. Differential count showed polynuclear leukocytes, 40 per cent.; small lymphocytes, 40 per cent.; myelocytes, 15 per cent.; mononuclears, 2 per cent. Death occurred on the fourth day after entering the hospital. Postmortem examination revealed greatly enlarged spleen and liver, the latter showing amyloid changes, but not siderosis; no enlarged lymph glands. The bone marrow of the femur in its lower one-third was red, in the upper two-thirds fatty. Microscopic examination of the spleen showed many small areas resembling abscesses, but cultures were negative. The case was believed to be one of grave infection of unknown origin.

Weber<sup>2</sup> describes a case in a man, aged fifty years, who came under his care complaining of weakness, anorexia, and tinnitus aurium. Physical examination showed the temperature 100°, the pulse 88, the radial artery sclerotic; and the skin very pale and yellowish. The liver reached from the eighth rib to navel, the spleen from the eighth rib to the crest of the ilium and to the right as far as the navel. There was slight edema of ankles. Blood examination: red cells, 1,800,000; white cells, 5000; hemoglobin, 25 per cent. Differential count showed polynuclear leukocytes, 37.5 per cent.; small lymphocytes, 49.4 per cent.; large lymphocytes, 10 per cent.; myelocytes, 3 per cent. Four megaloblasts and three normoblasts were seen in counting four hundred leukocytes. Poikilocytosis was pronounced. The patient died three weeks later. Postmortem examination

<sup>1</sup> Deut. Klin., 1902, Nr. 42.

<sup>2</sup> Brit. Med. Jour., June 18, 1904.

revealed greatly enlarged spleen and liver, no enlarged lymph glands, red metaplasia of the bone marrow, and hypertrophic hemolymph glands. Microscopically, bone marrow was found to be almost all fat, but it contained many nucleated red cells, some of which showed partially divided nuclei and multiple nuclei. The liver contained many myelocytes and nucleated red cells infiltrated between cords of liver cells; the spleen also contained many nucleated red cells.

Kirchensteiner's<sup>3</sup> case was a woman, aged forty-one years, coming under observation for weakness, headache, some pain in the bones, shortness of breath, and palpitation of the heart. She was well up to three weeks before entering hospital. Physical examination showed the skin pale, with somewhat yellowish tint; slightly enlarged heart dulness; the liver reached to level of navel; the spleen from eighth rib to ilium and to the right as far as the navel. The red blood cells were 885,000, the white blood cells 6700, the hemoglobin 18 per cent. A differential count showed polynuclear leukocytes, 77 per cent.; lymphocytes, 10 per cent.; myelocytes, 8 per cent.; large mononuclears, 4 per cent.; eosinophiles, 1 per cent.; normoblasts, 570 to the cubic millimeter; no typical megaloblasts. Five days later the red blood cells were 250,000, the white blood cells 53,000, the hemoglobin 16 per cent. A differential count showed much the same relationship as above, except that polynuclear leukocytes reached 78 per cent., while lymphocytes decreased to 5 per cent. The autopsy revealed nothing of importance.

Mosse,<sup>4</sup> reports the case of a woman, aged fifty years, who had been well up to about six months before coming under his care. She had become weak and pale, short of breath, and complained of loss of appetite. She had rather profused menstruation six months previously, and since then has not menstruated. Physical examination showed a pale, waxy skin; the spleen reached from the eighth rib to the anterior superior spine of the ilium and to the right as far as the navel; it was slightly sensitive to pressure. The liver was somewhat enlarged. Blood examination: red cells, 2,665,000; leukocytes, 30,870; hemoglobin, 50 per cent.; megaloblasts and normoblasts, very numerous. Differential count showed polynuclear leukocytes, 44 per cent.; mast cells, 5 per cent.; eosinophiles, 13 per cent.; myelocytes, 18 per cent.; eosinophilic myelocytes, 1.3 per cent.; lymphocytes, 3 per cent.; myeloblasts, 7.5 per cent. At the time this paper was written patient was still alive.

Teeter<sup>5</sup> reports a case with recovery in a child, aged ten years, in which megaloblasts and normoblasts were greatly increased, and accompanied by moderate enlargement of the liver and spleen.

<sup>3</sup> Münch. med. Woch., 1905, Nr. 21.

<sup>4</sup> Berl. klin. Woch., 1907, Nr. 49.

<sup>5</sup> Jour. Amer. Med. Assoc., February 16, 1907.

The number of white cells, 132,800, would tend to place this case at least on the border line.

The case reported by Luce,<sup>6</sup> Bushnell and Hall,<sup>7</sup> Morawitz,<sup>8</sup> and a few others do not seem to me typical. Preis<sup>9</sup> reports a case under the title of atypical leukemia, which, had the finding been described more in detail, might have belonged in this series.

The question as to whether or not leukanemia should be considered a clinical entity is worthy of further discussion. The cases here abstracted correspond rather closely, both as regards physical examination and blood findings, while several other cases, reported as leukanemia or atypical leukemia, gradually shade off toward the more typical leukemias, especially the acute myelogenous. The theory of Pappenheim<sup>10</sup> deserves consideration: he believes that leukanemia should not be considered a separate disease, but a combination of pseudoleukemia and myelocytosis; that the same cause which brings about any anemia may act as well in a case of pseudoleukemia; and that the same cause, in certain susceptible individuals, may bring about both conditions.

It is a matter of common knowledge that myelogenous leukemia is associated with considerable anemia and that the blood findings almost always show normoblasts and occasionally megaloblasts. Several authors have observed leukemic changes in the blood following infections, and this at times is accompanied by enlarged spleen.

Hunter<sup>11</sup> has demonstrated more or less clearly an infectious origin for pernicious anemia, and undoubtedly some cases with a clinical picture of pernicious anemia are due to infections. Certain toxemias also may be considered as a cause of pernicious anemia and of leukemia. The temperature at least in the cases reported as leukanemia is suggestive of an infection. Reasoning from this rather imperfect basis, it seems logical to suppose that while leukanemia has a very definite clinical and hematological picture, it is not a separate disease, but the result of some unknown infection which in certain individuals might cause an anemia, in others a leukemia, and in still a third class, who are especially susceptible, a clinical picture which combines the two. Further careful observations of cases of this character should throw considerable light on the etiology of both the leukemias and pernicious anemia.

I wish to express my gratitude to Dr. G. C. Crandall, through whose kindness I studied the case herewith reported.

<sup>6</sup> Deut. Arch. f. klin. Med., Band lxxvii.

<sup>7</sup> Edin. Med. Jour., 1906, p. 329.

<sup>8</sup> Deut. Arch. f. klin. Med., Band lxxxviii.

<sup>9</sup> Ztschr. f. klin. Med., 1905, lvii.

<sup>10</sup> Ztschr. f. klin. Med., 1904, lii.

<sup>11</sup> Brit. Med. Jour., November 9, 1907.

## THE PATHOLOGICAL ANATOMY OF BRONCHIAL ASTHMA.

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OWING partly to lack of definite knowledge regarding the pathological anatomy of bronchial asthma, various theories have been advanced concerning its nature. The explanations given by different clinicians may be placed in three groups:

1. *Spasm of the Diaphragm.* First propounded by Wintrich, this theory has been supported by a number of later writers. Riegel and Edinger<sup>1</sup> conclude that spasm of the diaphragm, more than spasm of bronchial muscles, plays an important part in asthmatic attacks. Their opinion was based on experimental studies, and possibly is entitled to more than usual attention, because they had fully expected to prove exactly the opposite. More recent writers are in general not favorably inclined toward this view.

2. *Spasm of the Bronchial Muscles.* This view of Biermer's<sup>2</sup> still has many adherents, some holding it to be the principal feature, others at least a part of the asthmatic phenomenon. Riegel and Edinger state that their own and other experiments indicate with certainty that the smooth muscle fibers of bronchi contract upon irritation of the vagi; that this is the cause of asthma, however, is not proved. Their view that this is less important than spasm of the diaphragm has been mentioned. Lazarus,<sup>3</sup> from experiments on rabbits, concludes that both bronchospasm and asthmatic catarrh are necessary to produce bronchial asthma. Talma<sup>4</sup> regards the affection as primarily due to spasm of the muscles of the respiratory tract. These muscles are, to a certain extent, under control of the will, or can be brought under control, hence his method of treating the disease by respiratory gymnastics. Aufrecht<sup>5</sup> convinced himself that the musculature of the finer bronchi consists (as in animals) of a stout layer of circular and a much weaker layer of longitudinal fibers, the effect of the contraction of which is evident. Nevertheless, he does not admit that asthma must be regarded as a consequence of bronchial muscle cramp, since the affection may be due to catarrh of the finer bronchi.

<sup>1</sup> Ztschr. f. klin. Med., 1882, v, p. 413.<sup>2</sup> Volkmann's Samml. klin. Vorträge, 1870, Nr. 3.<sup>3</sup> Deut. med. Woch., 1891, Nr. 27, p. 852, and Nr. 36, p. 1057.<sup>4</sup> Berl. klin. Woch., 1898, Nr. 52, p. 1141.<sup>5</sup> Deut. Archiv f. klin. Med., 1900, Band lxxvii, p. 586.

Fraenkel<sup>6</sup> says the theory of bronchial muscle cramp explains, for the most part, the phenomena of the asthmatic attack, and experimental physiological investigations regarding contractility of the bronchi give this some support. These investigations, however, give too little consideration to undoubted changes in the bronchial mucous membrane. Elsewhere, in discussing the mechanism of spiral formation, he assigns a necessary function to bronchial spasm, stating that, in addition to the tenacity of the bronchial secretion, at least an indirect part is taken by such contraction. The latter, narrowing the bronchial lumen, has to do with consistence of the mucus, and interferes with the passage of air. When this spasm fails, as in ordinary asthma, tenacious sputum alone is not formed into spirals.

Pieniazek<sup>7</sup> regards the view that attacks of bronchial asthma are due to cramp of small bronchi as not tenable; much more probably are they due to swelling of the mucous membrane in the smaller bronchi. Grossmann<sup>8</sup> says the power of contractility of the bronchial muscles can be no longer denied. This is, however, by no means strong enough in itself to produce a grave respiratory disturbance. Experimentally it is not possible to produce contractions of the bronchi without at the same time causing circulatory changes in the pulmonary vessels. Clinically, doubtless these two conditions always run parallel. On the other hand, changes in the pulmonary circulation can, experimentally as well as clinically, appear without contraction of the muscles. Upon the degree and rapidity of onset and disappearance of this circulatory change depend also the degree and acuity of the respiratory disturbance.

3. *Bronchial Catarrh.* That this condition forms a large, if not indeed the principal, part of the pathology of bronchial asthma is believed by many observers, some of whom have been quoted in the preceding paragraphs. Fraenkel says that mere catarrh of the finer air passages is to be rejected as the only cause of asthma, because it furnishes no basis for the suddenness of the attacks. It is doubtful if in all cases catarrh goes before spasm of the muscles, although it appears plausible that spasm of muscles might easily follow when bronchioles are partly closed by swelling of the mucosa and the presence of tenacious content. Pieniazek, in upholding this theory, states that swelling of the mucous membrane can occur very quickly, as is seen in cases of oedema of the uvula, in urticaria, etc. Retardation of expiration is better explained by this than by muscle cramp. Pathologically he regards asthma as standing between pure oedema and acute catarrh. To paralysis of the small bronchial veins he assigns the swelling of the mucous membrane.

<sup>6</sup> *Spezielle Pathologie u. Therapie der Lungenkrankheiten*, 1904.

<sup>7</sup> *Wien. klin. Woch.*, 1905, Nr. 46, p. 1201.

<sup>8</sup> *Ztschr. f. klin. Med.*, 1907, Band lxii, p. 179.



Aufrecht believes that asthmatic attacks of a day and longer are better explained by assuming the presence of catarrh.

Whatever the changes in the bronchi, or the diaphragm, may be, they apparently are the result of a primary disturbance in the nervous system. Hoffmann<sup>9</sup> states that by asthma we understand a neurosis in the domain of the respiratory nerves, which shows itself by attacks of dyspnoea, with characteristic secretion and distention of the lungs; the affection is, perhaps, a pathological change in the respiratory centre of the medulla. Fraenkel's view is that the asthmatic patient has to charge for the greater part, probably even exclusively, the peculiar condition of his nervous system as the source of his disease. In the majority of instances this condition is a hypersusceptibility of that portion of the nervous system which is in direct relation to the respiratory tract. In a series of cases the responsible focus is a circumscribed area which, through gradual pathological changes, becomes an irritation point, from which attacks develop, as in many forms of nasal asthma. In a second type there is increased irritability of the collective mucous surface from the nose to the bronchi, and in a third there possibly exists a similar condition in the bulbar respiratory centre. Finally, in a minority of cases, the remainder of the nervous system may be at fault, as in asthma, which is one of the phenomena of general neurasthenia. With right, therefore, he says, asthma may be designated a reflex neurosis.

Materials from which to determine the pathology of asthma are principally two—the sputum ejected by persons suffering from the disease, and the lungs of those who die during an attack. The former, largely a clinical question, about which a great deal has been written, I shall later discuss briefly in connection with certain points relating to lesions found in the lungs. As regards the latter, I have found in literature the reports of but seven cases in which histological studies were made of the lungs of asthmatic subjects who died during an attack of that disease. The findings in these may be thus briefly summarized:

CASE I (von Leyden<sup>10</sup>).—Female, aged forty years. From childhood had almost daily attacks of asthma. Died in an attack during cyanosis, dyspnoea, and stertor. At autopsy a high grade vesicular emphysema of both lungs was found. The bronchi were not dilated; the mucosa was reddened, but not otherwise abnormal. Microscopically some of the alveoli were dilated; others were not. They were filled with granular material in which was embedded a moderate number of large cells. In the smaller bronchi was a similar material tightly adherent to the walls and narrowing the lumina; at one point this substance formed a plug-like mass that

<sup>9</sup> Nothnagel, Spec. Path. u. Ther., Band xiii.

<sup>10</sup> Deut. Militärärztl. Ztschr., 1886, Heft ii.

completely occluded the bronchus. Neither fibrin nor Charcot-Leyden crystals were found in this mucous material occupying the bronchi. The walls of the bronchi were not essentially changed.

CASE II (Berkart<sup>11</sup>).—Female, aged thirty-seven years, who had suffered from attacks of asthma during a period of fourteen years, finally dying in a state of dyspnoea and general congestion. Autopsy showed hypertrophy and dilatation of the heart and emphysema of the lungs. In the right primary bronchus was a dark brown clot-like plug, almost closing the lumen; a similar mass was in a branch of the left bronchus. Many of the smaller bronchi were not only dilated, but were also partly occluded by exudate. Microscopically the epithelium was absent from the wall of the right bronchus over the area in contact with the plug, and also from the smaller bronchi, where there was an ostensible fibrinous exudate. The medium sized bronchi were more or less nearly filled by detritus-like masses, in which were fragments of Charcot-Leyden crystals. The brownish clot in the right bronchus consisted chiefly of degenerated epithelium in connection with spirals. Among the epithelium were cylindrical types which showed change into thread-like forms of variable length, some of these appearing as whip-like projections on fairly well preserved cells. Similar long-drawn-out cells had also been found in the sputum. A part of the emphysematous pulmonary alveoli contained fibrinous exudate.

CASE III (Schmidt<sup>12</sup>).—Female, aged forty-nine years, who had developed asthma in addition to a medullary carcinoma of one lung. Patient died during a severe exacerbation of an attack lasting a week. Section of the lungs showed that the peripheral somewhat dilated bronchi of the upper lobe of each were surrounded by grayish pigmented, strongly compressed tissue here and there beset with caseous foci. They contained spiral-formed mucous threads, which were unusually adherent to the walls, but could by forceps be drawn out in masses many centimeters long. Microscopic examination showed that in the majority of the small dilated bronchi the epithelium was well preserved. By the application of various staining methods (Weigert's thionin, triacid) it was clearly demonstrated that the content was, for the greater part, mucus, with a few cellular elements and Curschmann's spirals. The spirals diminished toward the periphery, and only in certain places could a turned appearance of the content in the respiratory bronchioles be noted. Nowhere in the considerably dilated alveoli could a spiral be found. The mucosa and submucosa were infiltrated by round cells. For the greater part the lumina were entirely filled with a homogeneous material in which were embedded, in addition to spirals, various types of cells. These included alveolar epithe-

<sup>11</sup> On Bronchial Asthma, 1889, 2d edit.

<sup>12</sup> Ztschr. f. klin. Med., 1892, Band xx, p. 476.

lium, a moderate number of leukocytes with lobed nuclei (but none with eosinophile granules), homogeneous, round, oval, or spindle cells, with neither nuclei nor granules, and epithelial cells, sometimes in masses. The content of the ducts of the mucous glands showed no especial consistence or winding, though the glands were in strong secretion. As typical central threads were found also in the smaller glandless bronchi, it was evident that they were a secretory product of neither the mucous glands nor their ducts. Surrounding the mucus-filled bronchi were areas of considerable alveolar dilatation; these alveoli contained a slight amount of granular material or were entirely filled with a substance resembling that in the bronchi and shown by thionin and triacid to be mucus. The bronchi containing no mucus were empty or contained cells the larger number of which were polynuclear leukocytes. Surrounding the latter bronchi were bronchopneumonic areas; that is, the septa were infiltrated, the alveoli were emphysematous, and in them were many alveolar epithelial cells and leukocytes without intercellular material.

CASE IV (Fraenkel<sup>13</sup>).—A man aged sixty-three years, who, during his last year, had many attacks of asthma. At autopsy both lungs were found widely expanded, meeting in the middle line. In the left primary bronchus was a large quantity of thin mucous fluid. The lung was largely air-containing, and on the border were many cherry-sized emphysematous vesicles. The bronchial mucous membrane was strongly reddened, the lumina were dilated, and in part filled with tough masses which could be pulled out in the form of thready clots. The right lung possessed extensive adhesions, and the cut surfaces showed marked œdema. The bronchi were widened and contained material similar to that in the left. The walls of the larger bronchi were thickened and at points showed scars and lime deposits. The bronchial glands were large and pigmented.

In stained sections from the bronchial clots typical large spirals were not seen, but instead a large number of thready, in part wound, formations, staining blue, and not entirely homogeneous, but slightly granular in appearance (fibrin?). Other similarly formed clots consisted of cylindrical epithelium, in part close together, in part irregularly placed, in part palisade-like, as before desquamation. In a few was a suggestion of winding. Eosinophiles were not perceptible.

Microscopic examination of the tissue showed a high-grade desquamative bronchial catarrh. The cylindrical epithelium was detached and filled the lumina, being in part in serpentine form, in part as distinct bands around a central axis. These cell accumulations were in some places so great as to fill the bronchial

lumen. The vessels of the mucous membrane were dilated, the peribronchial tissues infiltrated with small cells. In consequence the denuded mucous membrane was at points elevated, and the bronchial wall appeared not inconsiderably thickened. The lung was in part normal, in part emphysematous, with, at points, increase of interstitial and interalveolar tissues. In many places alveoli were filled with blood, and in others, in the vicinity of dilated bronchi, the lumina and walls were so filled with lymph cells as almost to arouse the impression of beginning suppuration. At other points the lungs showed atelectasis, partly due to dilatation of bronchi, partly to increase of connective tissue.

CASE V (Fraenkel<sup>14</sup>).—A woman, aged forty-eight years, who, at various times, suffered from asthma, during the last period being under observation for more than a year. Attacks occurred almost daily. The tenacious sputum contained numerous coagula, with Curschmann's spirals and asthma crystals therein. The last typical attack occurred thirty-six hours before death. In spite of this the majority of middle-sized and small bronchi were found at autopsy to be filled with exquisite screw-shaped coagula, some many centimeters in length. Sections of the lung were stained by a modification of the Biöndi-Heidenhain method, and showed, as did Schmidt's, that the bronchial effusion was entirely of mucus. In many of the dilated small bronchi were spiral figures whose centres stained the same as the mucous cell content of the epithelium lining the tube, while the mesh-like spaces of the periphery contained numerous eosinophiles.

The genesis of the coagula in the small bronchi of 0.15 to 0.3 mm. lumen could be distinctly followed. First was a considerable increase in the ciliated cells of the epithelial covering, of which isolated cells throughout were very much longer than the normal, the transverse diameter being correspondingly diminished. Some cells were 20 microns high. The nuclei were still normal. Mucus protruded from the cell bodies and into the lumina of the bronchioles or passed over directly into spirals. At many points, in some over the entire circumference, numerous large epithelial cells were loose and so far from the wall that three or four lay behind each other. These free cells were drawn out, in part large spindle-formed, and showed on the end toward the bronchial wall whip- or awl-like thin projections, which lost themselves between the cells that were not so greatly changed and were still attached to the wall. Other changes in the bronchi were hyperemia of the mucous membrane, with small blood extravasations, and the specially striking appearance of numerous heaps of closely placed leukocytes in the thickened walls of the bronchioles. These cells were largely eosinophiles, of which the majority were mononuclear, similar to

those already mentioned as in the lumina of the bronchi. In the immediate vicinity of the eosinophiles, and in part surrounded by them, were groups of well-formed Charcot-Leyden crystals.

CASE VI (Jezierski<sup>16</sup>).—A man aged sixty-three years, whose father also died of asthma. Had first attack in 1900, followed by others in 1903 and 1904. Died of right-sided pneumonia in two days while under treatment for asthma. At autopsy the right lung was large and heavy, the middle and upper lobes liver-like in consistence. The left lung was small, light, slightly pigmented; the bronchi were dilated, their mucosa red. The cut surfaces of the right upper lobe were dark red and covered with foamy fluid; of the middle lobe, grayish yellow to red, and with protruding granules. Isolated, many-branched fibrin plugs were in the small bronchi. Material saved for microscopic study included medium and smaller bronchi of the left lung, pieces of the right lung, diaphragm, and both phrenic and vagi nerves.

Microscopically the bronchioles showed in the lumina closely crowded cell masses in addition to well-preserved cells, chiefly ciliated epithelium, which singly or in rows had desquamated or remained hanging to the basement membrane by long thin stalks; among them were also round, non-ciliated epithelium, numerous leukocytes, lymphocytes, erythrocytes, and eosinophiles, all embedded in a ground substance which was shown to be mucus. Fibrin was not demonstrated. At the basement membrane the epithelium was well preserved, though between the elements were round cells. The latter were also numerous in the walls and peribronchial tissues, some diffusely placed, some in heaps, arranged in part like lymph nodes. The quantity of elastic tissue was unusual, far exceeding that in the lungs of other individuals of the same age, and of arteriosclerotic persons, with which they were compared. Also unusual was the presence in the bronchial walls of an abundance of small bloodvessels. On transverse section of the bronchi these vessels appeared closely crowded together, forming, as it were, a palisade-like wall around the tunica propria. In some of the vessels were isolated fibrin threads. In the perivascular lymph spaces were numerous cocci, mainly diplococci; these were also found sparsely in the lumina of the bronchioles. The peribronchial tissues were likewise infiltrated by round and blood cells. Study of the diaphragm and the neck muscles showed rarification and fatty infiltration of the former; otherwise nothing abnormal. The vagi and small nerves of the neck were intact. The phrenic nerves showed, by Marchi and Flemming safranin staining methods, some changes, a part of the fibers being tinged blackish brown, or swollen or notched in a bead-like manner. The right lung showed a typical pneumonic condition.

CASE VII (Jezierski).—Female, aged forty-six years, who had attacks of asthma for twelve years, death from dyspnoea occurring during an attack. In each pleura was, approximately, 200 c.c. of bloody serum. The left lung was markedly emphysematous, but on section showed a good blood content. On pressure there flowed from some bronchi small, worm-shaped, quite consistent mucous masses. The right lung on section showed somewhat smaller worm-shaped structures, but otherwise was like the left. Small pieces of these clots examined fresh showed an enormous quantity of epithelium, mostly ciliated, with long clear nuclei and heavy cilia. The majority were striking because of their unusual narrowness and length, especially the end threads, which often reached one-third the diameter of the field ( $\frac{1}{2}$  oil immersion), as already described by Berkart and Fraenkel. In addition was cuboidal epithelium from the deeper layers, numerous round cells, isolated red cells, and masses of detritus. In sections of the clots the nuclear structure and narrowness of the thread-formed epithelial cells did not show so clearly; there appeared here numerous eosinophiles, round and polygonal epithelium, many with two nuclei, pale, barely tingibile cell remains, and, as ground substance, mucus.

The bronchi, on transverse and longitudinal section, showed mostly intact and undamaged epithelium. Only in isolated places was it detached or broken through by masses of round cells. These penetrated between the epithelial cells as rows, passed into the basement membrane, and infiltrated widely the bronchial walls and peribronchial tissues, either diffusely or in isolated masses. In part they were small, mononuclear, with scanty protoplasm, but the majority were larger, with dark, indented nuclei and abundant protoplasm; they were most numerous in the vicinity of vessels. The smaller the bronchus the more numerous were the cells, often so many in the lumen and surrounding tissues that the bronchial structure was not clear. The elastic tissue was in this case not increased, neither was there the new vessel formation as in the first. The pulmonary parenchyma was intact.

Through the courtesy of Professor Dr. Stadelmann, Director of the Department of Internal Diseases, and of Dr. Pick, Prosector of the Friedrichshain Hospital, I am enabled to add to this list another case. To both these gentlemen, and especially to Dr. Pick, for his kind supervision of my work, I hereby express my warmest appreciation and thanks.

CASE VIII.—O. S., a coachman, aged twenty-seven years, was admitted to the hospital April 2, 1907, and died on the following day. Owing to the severe dyspnoea of the patient, his previous history could not be obtained from him, but later was ascertained through the courtesy of Dr. Carl Bruck, of Berlin, who had treated him during the previous year for attacks of bronchial asthma. The man had also exhibited tachycardia, but neither Dr. Bruck

nor a consultant from the University of Berlin could discover a lesion referable to the heart. Neither considered the attacks of asthma as being in any way related to the heart, regarding them, therefore, as pure bronchial asthma. At the time of admission the face and extremities of the patient were strongly cyanotic; oedema was not present. There was severe expiratory dyspnoea, with coughing expiration. The asthmatic attack continued almost unbroken through the day and night and until evening of the following day, when the symptoms abated and the patient slept. At 9 P.M. he suddenly collapsed and died. The clinical diagnosis was bronchial asthma and heart failure.

At autopsy the anatomical diagnosis was: Hypertrophy of left ventricle; dilatation of right ventricle; pulmonary emphysema; purulent bronchitis; exudative bronchiolitis. The body was that of a strongly built man. With exception of the face, cyanosis was marked. The lungs were distended, entirely covering the pericardium. The heart was of good color, the wall of left ventricle 1.5 cm. thick, the right ventricle somewhat dilated, and the muscle flabby. The valves were smooth. The right lung was slightly adherent to the thoracic wall, greatly inflated, soft, and easily indented. On section the organ was strongly red in color and not of excessive air content. By pressure on the lower lobe pus could be expressed from the bronchi. The bronchial mucous membrane was red in color. On the cut surfaces of the lung could be seen numerous shiny, often greenish colored mucous plugs, which protruded from the finest bronchial branches. There were also fine, worm-like, mucous clots 2 to 3 cm. long, corresponding to the small mucous-filled bronchi. The larger masses of mucus were yellowish green in color, those in the finer bronchi more whitish and clear in appearance. The left lung was not adherent to the thoracic wall, but otherwise was like the right.

The material studied histologically consisted of several blocks of tissue from various parts of each lobe of both lungs; after fixation by Zenker's fluid, it was hardened in alcohol, and finally embedded either in paraffin or celloidin. Numerous sections from each were stained by hematoxylin, with the addition of eosin or Van Gieson, Schmidt's and Fraenkel's modifications of the Biondi-Heidenhain method, Weigert's elastica, Gram-Weigert, and thionin.

Microscopically, the lumina of the majority of the smaller bronchi possessing a diameter of from 0.13 to 0.16 mm. are partly or entirely filled with material which, in different places, varies slightly in its constituents. In general there is a ground substance, slightly granular or almost homogeneous in appearance, in which, at points, are embedded a few cells. Staining by Biondi-Heidenhain and thionin shows in every instance this substance to be mucus. In sections from some of the blocks are bronchi in which this mucus is arranged in distinct spiral form. In these formations the central

portion is quite dense and homogeneous, staining deeply and uniformly; the peripheral parts are less dense, and react less intensely to stains. The latter portions contain a variable number of cells, which become more numerous as the wall of the bronchus is approached. A few of these cells are mononuclear, and appear to be the remains of partially degenerated epithelial cells, *but desquamated epithelium is in these bronchi exceedingly scanty, those cells*



FIG. 1.—Bronchus of 0.3 mm. lumen containing three spirals in cross-section. The epithelium is intact, except on the left where the wall has been mechanically torn. (Leitz ocular 1, objective 3.)

*in general being still attached to the wall.* Instead of being elongated, they are either of normal appearance or are even flattened by the exudate, the average height being 7 microns. The majority of the cells in the lumen, and they are numerous in none of the bronchi of this size, are polynuclear leukocytes. Occasionally is seen an eosinophile, but those cells are nowhere numerous, and none has been observed directly within a spiral; they are polynuclear in type.



In bronchi of larger size, from 0.2 to 0.45 mm. in diameter, with, at points, well-preserved epithelium, are also spiral formations (Fig. 1), or isolated central "threads" or a granular material, in which are, at points, fairly numerous cylindrical epithelial cells; *the latter show no elongation*, measuring 13 microns in height. Some of these are irregularly placed, while others still bear the same relation to each other as before desquamation, appearing as palisade-like masses placed at some little distance from the basement membrane, and forming a boundary to the central mucous content of the tube; the space between these cells and the bronchial wall is in many instances entirely clear. In the central parts are isolated epithelial cells and enormous numbers of polynuclear leukocytes, eosinophiles being few or absent. In some of these bronchi the entire lumen is filled by a mass of polynuclear leukocytes, granular material between them being very scanty. At certain points the



FIG. 2.—Elongated desquamated epithelial cells from the bronchial mucosa.  
(Leitz ocular 1, objective 7.)

epithelial lining has disappeared and the content of the lumen merges gradually, almost imperceptibly, with the greatly infiltrated bronchial wall. At one point hemorrhage has occurred into the bronchial lumen, from an eroded vessel. In such of these bronchi as contain considerable quantities of mucus, this material is arranged in the form of definite striæ running in the longitudinal axis of the lumen, the contained leukocytes also showing a similar linear arrangement. In many places the polynuclear cells are all thus placed in rows in which the individual cells are nearly or quite in contact.

In other still larger bronchi, with lumina of 0.8 mm., are small or greater quantities of mucus and desquamated epithelial cells. Some of the latter are distinctly elongated (see Fig. 2), reaching a length of 35 microns, *but these are only isolated cells, scattered here and there among a much greater number normal in length.* In only

a few instances do these cells appear similar to those pictured by Fraenkel, and then are in no way equal in quantity or regularity to those found in his case. They lack entirely a definite relation to the mucus contained in these bronchi. In some bronchi of this size eosinophiles are fairly numerous. Charcot-Leyden crystals have been seen in none of the specimens.

The walls of the bronchi, especially the smaller, are markedly infiltrated by leukocytes. Those immediately beneath the basement membrane are, in all instances, almost exclusively polynuclear in type; external to the muscle coat mononuclears, mainly large, with vesicular nuclei, are in evidence, but even here the polynuclears are in many places numerous. These cells in some locations extend to a few of the surrounding alveoli, giving the suggestion of small foci of peribronchial pneumonia. Among the cells in the bronchial walls are also eosinophiles, all polynuclear in type. In some bronchi they are scanty, and in others, especially the middle-sized, very numerous; in one of the latter are thirty-six in one field of the Leitz  $\frac{1}{2}$  oil immersion, ocular 1. The vessels of the bronchial walls are dilated and filled with red cells. The leukocytes in them are considerably increased in number, and in many vessels are distinctly marginal in location; eosinophiles have not been seen in these vessels. Minute hemorrhages in the bronchial walls are occasionally found, but are not at all a prominent feature. In some of the larger bronchi the basement membrane and tunica propria show pronounced hyaline degeneration. The muscles appear unchanged and there is no appreciable increase in the connective tissue of the walls. The elastica likewise is apparently normal.

The parenchyma of the lungs shows some changes. In many parts the alveoli are distended, with, in some instances, rupture of the walls and consequent formation of variously sized emphysematous spaces. The alveolar capillaries are quite uniformly engorged. Alveoli bordering the bronchi and containing mucus and leukocytes have been mentioned, but at some points not in demonstrable relation to bronchi are groups of several alveoli each that are partly or almost entirely filled by mucus, in which are embedded numerous leukocytes (90 per cent. polynuclear), desquamated alveolar epithelium, and red blood cells. This material is slightly more granular than is that in the bronchi, and also lacks the striation of the latter. In alveoli in various parts of the sections, some containing but little exudate, are polynuclear eosinophiles in numbers varying usually from one to four to the alveolus, but in one instance an alveolus contains eleven of those cells.

The larger bloodvessels of the lung show in general no striking change, except all contain more than the usual amount of blood. Many contain small quantities of fibrin, a few even small coagula of fibrin and leukocytes. In sections from one block, however, is

a medium-sized vessel containing a plug of leukocytes, essentially all polynuclear in type. This vessel extends in one section half the width of the field of a Leitz objective 3, ocular 1, and is throughout almost solidly filled by leukocytes, containing only at points a few red cells. Isolated small arteries show splitting and fragmentation of the inner elastic lamina in part of their circumference; one vessel has attached to this portion of its wall a small thrombus.

In comparison with previously reported findings, the prominent features of this case are: (1) The presence of mucus in the finer bronchi, with the formation therein of spirals. For the formation of these bodies the coöperation of cells appears not to have been essential, since desquamation of epithelium is here slight or entirely lacking, and leukocytes are present only in small numbers, and chiefly at the periphery of the spirals. The cylindrical epithelial cells of these bronchi are not elongated, but, on the contrary, are, at points, flattened by the exudate. (2) In bronchi of larger size the epithelium is partly or entirely desquamated, and polynuclear leukocytes appear in large numbers, both of these elements being added to the mucus or spirals, as the case may be. (3) In some of the middle-sized bronchi a few of the cylindrical epithelial cells show elongation, but this is in no instance a regular or prominent feature.

Collectively these reports of autopsy findings show that *the pathological anatomy of bronchial asthma is not the same in all cases*, though in some points they quite closely correspond. Later writers agree that the essential process is in the finer bronchi, and not the alveoli, though v. Leyden<sup>16</sup> expressed the belief that lymph-like fluid passes into the alveoli, and in part into the smaller bronchi, and there coagulates. Riehl's cases, mentioned later, are apparently an exception to this statement regarding location of the process, but since his view, well founded clinically, lacks the support of histological study, it cannot be accepted as negating actual tissue findings. The later cases also agree in the bronchial content being mucus instead of fibrin. Desquamation of bronchial epithelium, though present in most cases, varies considerably as regards location and extent. Fraenkel regards the desquamation of epithelium in the smaller bronchi as one of the two essential features of asthmatic catarrh, and his cases lend weight to that view. On the contrary, in the case of Schmidt, Jezierski's second case, and in mine, the epithelium in the finer bronchi was in general well preserved. This point is of special interest in its bearing upon the part taken by these cells in the formation of spirals, Fraenkel believing that the central threads, not improbably the "free" threads, and naturally a part of the centre of the spirals, are formed from the elongated ciliated epithelial cells.

<sup>16</sup> Deut. med. Woch., 1891, Nr. 37, p. 1085.

TABLE GIVING SUMMARY OF THE FINDINGS IN THE EIGHT REPORTED CASES OF BRONCHIAL ASTHMA COMING TO AUTOPSY.

Case.	Lungs macroscopically.	Bronchial lumina microscopically.	Bronchial content.	Bronchial epithelium.	Bronchial wall.	Pulmonary alveoli.
I. Female, 40 years. v. Leyden (1886).	High grade vesicular emphysema. Bronchi not dilated; mucosa reddened, but not essentially changed.	In smaller bronchi narrowed by content; at one point, plug-like filling.	Granular material in which moderate number of large cells are embedded. Mucosa no fibrin; no crystals.	.....	Not essentially changed.	Some alveoli dilated, some not; some contain granular material and large cells.
II. Female, 37 years. Berkart (1889).	In right primary bronchus and branch of left, dark brown plugs. Many small bronchi dilated and partly occluded by exudate.	Medium sized more or less occluded.	Ostenible fibrinous exudate in smaller. Detritus-like masses with fragments of Charcot's crystals in medium. Degenerated epithelium and spirals in large.	Desquamated where the exudate is in contact.	.....	Some of dilated alveoli contain fibrinous exudate.
III. Female, 49 years. Schmidt (1892).	Peripheral bronchi somewhat dilated, and contain long, spiral, mucous threads, quite tightly adherent to wall.	Small for greater part entirely occluded.	Homogeneous mass, in which are alveolar and bronchial epithelium, polynuclear leukocytes, round, oval, or spindle cells and spirals. Mucous. No eosinophile granules.	Well-preserved in majority of small dilated bronchi; at points absent.	Mucosa and submucosa infiltrated with round cells.	Alveoli in some places contain material same as in bronchi (mucus). Bronchopneumonia around some bronchi.
IV. Male, 63 years. Fraenkel (1898).	High-grade emphysema. In left primary bronchus large quantity of thin mucous fluid. Bronchi dilated; mucosa reddened.	In medium and smaller, plug-like occlusion by elongated cylindrical epithelium.	Partly wound threads. Granular material (fibrin?) Cylindric epithelium. No eosinophiles.	High-grade desquamation.	At points thickened. Vessels dilated. Peribronchial tissues infiltrated by round cells.	Some alveoli contain blood some lymph cells. Emphysema in parts, atelectasis in others.
V. Female, 48 years. Fraenkel (1900).	Middle-sized and smaller bronchi filled with long, screw-shaped coagula.	Majority of small and middle-sized occluded.	Mucous. Spirals. Desquamated epithelium. Numerous eosinophiles.	Pronounced elongation and desquamation.	Hypertemia and small hemorrhages. Numerous leukocytes, largely eosinophiles; near them Charcot-Leyden crystals.	

VI. Male, 63 years. Jesierski (1905).	Right, pneumonia (hepatized). In left, small bronchi dilated, mucosa reddened.	Bronchioles filled with exudate.	Mucus. Ciliated epithelium, leuko- and lymphocytes, erythrocytes and eosinophiles.	Superficial desquamated, lower layers well preserved.	Numerous round cells in wall and peribronchial tissues. Elastica increased. Many new bloodvessels. Numerous diplococci in perivascular lymph spaces.	Remained intact.
VII. Female, 46 years. Jesierski (1905).	Left, markedly emphysematous. Worm-shaped mucous masses from small bronchi of both lungs by pressure.	Smaller large lymphoccluded by round cells.	In clots examined separate from tissue are numerous elongated cylindrical epithelial cells and eosinophiles. Mucus.	Only in isolated places detached.	Enormous number of round cells, mainly large in size.	
VIII. Male, 27 years. Ellis (1908).	Emphysematous. Fluid (pus) in larger bronchi. Mucous plugs in small bronchi. Bronchial mucosa reddened.	Most of smaller partly or entirely occluded by exudate.	Mucus. Cylindric epithelium in middle and larger. Polynuclear leukocytes. Few polynuclear eosinophiles. Spirals. No crystals.	Extensive desquamation of cylindrical cells in middle and larger, not in finer bronchi.	Infiltrated by leukocytes, mostly polynuclear. Many eosinophiles. Hypermia. Hyaline degeneration of basement membrane in large bronchi. Elastica not increased.	Vesicular emphysema. Exudate in small areas. Eosinophiles in alveoli.

These elongated cells had been noticed by Berkart, who suggested the possibility of their forming spirals; Fraenkel stated that his case is the first in which this formation has actually been demonstrated. *That this is not the method in all instances, however, is shown very clearly in my experiments with spirals formed from mucus in small bronchi in which epithelial desquamation had not occurred.*

In other respects, as regards the number and type of leukocytes, the presence of Charcot-Leyden crystals and eosinophiles, elongation of epithelial cells, and changes in the component parts of the bronchial wall, the cases differ widely. In the accompanying table I have stated briefly the findings in each of these respects, and the points of resemblance and difference may there be noted. Jezierski, from a comparison of his cases, tentatively concludes that equally typical symptoms of bronchial asthma can be drawn out through at least two different originating conditions, and that, therefore, there is not a uniform etiology of those symptoms. Fraenkel also states that comparison of his two cases shows that, during asthmatic attacks, the pathological anatomy is not in every case the same. He, however, regards as a common band uniting them all the extensive epithelial desquamation in the bronchioles, the other essential feature being the secretion of unusually tenacious mucus. I have already shown that the former cannot be regarded as a common and essential feature, since it is not present in all cases.

*The findings in the lungs, therefore, explain the sputum of bronchial asthma only to a very limited degree.* This is not surprising in view of the fact that the term "characteristic," so often applied to the material expectorated by persons suffering from this disease, is a misnomer. Viscid mucus is possibly the most constant constituent, and in it may be embedded epithelial cells, leukocytes of various types, eosinophile cells, Charcot-Leyden crystals, and spirals. When all these are present a quite striking picture is produced, but one or more of these elements may be lacking, and, what is of much greater importance, almost identical material has been expectorated by persons suffering from other affections. Kaufmann<sup>17</sup> states that spirals are found in the sputum of other diseases of the lungs, as croupous pneumonia and bronchopneumonia, fibrinous bronchitis, and pulmonary oedema. He has repeatedly found them in the tough mucus behind stenoses of the bronchi, due to anthracotic bronchial lymph nodes or to tumors, primary or secondary, of the bronchial wall. Each of the other elements mentioned has also been found in the sputum in connection with diseases other than bronchial asthma.

With the possible exception of Fraenkel's one case, the reported tissue studies furnish cumulative evidence that spirals are formed from mucus. Schmidt says no doubt has existed about the mucous

<sup>17</sup> Lehrbuch der spez. Path. Anatomie, 1907, Auf. 4, p. 204.

nature of the outer spiral windings, but there has about the central thread. He concludes that at least the typical Curschmann spirals possess also a centre of mucus, and therefore have nothing to do with fibrin. He, however, found fibrin masses in the sputum of six or eight cases of asthma, but always sharply separated from the accompanying spirals. Even these findings are so at variance with other reports that later writers justly regard them as strongly suggestive of cases of fibrinous bronchitis. Schmidt's statement that the best method of demonstrating spirals in sections of sputum is the use of Weigert's fibrin stain also permits criticism of his findings, even though he decolorizes the sections until only a pale blue shimmer remains. I am quite convinced that errors in differentiating fibrin and mucus arise from the use of this stain, whatever the details of the technique may be. This possibility I proved to my own satisfaction with material from the case reported. Staining with a weak solution of thionin and examining the section under water, as recommended by Schmorl, I find one of the best methods of demonstrating mucus in tissues. To avoid the use of alcohol entirely, Liebermeister,<sup>18</sup> before removing the paraffin, stains sections for five minutes with a weak solution of thionin, removes the paraffin with xylol, and mounts in balsam. This method gives fairly satisfactory results.

Schmidt's modification of the Biondi-Ehrlich-Heidenhain stain for tissue sections, as given by Fraenkel, is as follows: A stock solution is made by dissolving 1 gram of the mixture in 30 c.c. of distilled water and allowing this to stand for some time. The staining fluid is then made by taking of the stock solution 2 c.c., distilled water 40 c.c., 0.5 per cent. acid fuchsin solution 3 c.c., and 0.2 per cent. acetic acid solution 4 drops. In this the sections are placed for twenty-four hours, rapidly washed with 90 per cent. alcohol, dehydrated in absolute alcohol, cleared in xylol, and mounted in balsam. Fraenkel, after washing with 90 per cent. alcohol, stains one-half minute with 1 per cent. iodine-green in 2 per cent. carbol water, differentiates in 90 per cent. alcohol until neither red nor green color appears, and completes the mounting as already given. Mucus is stained green, and, at least in my sections containing fibrin in the bloodvessels, fibrin a purplish violet. Eosinophiles are well stained.

Predtetschensky<sup>19</sup> examines sputum by placing it on a black surface and isolating the characteristic flecks. These are placed on a slide and a cover-glass pressed down upon them. When spirals are found microscopically, the cover is slid off and the slide dried in air. The after-steps are: (1) Fix in methyl alcohol three to five minutes; (2) dry in air; (3) stain thirty to fifty minutes with (a)

<sup>18</sup> *Deut. Archiv f. klin. Med.*, 1904, Band lxxx, p. 551.

<sup>19</sup> *Ztschr. f. klin. Med.*, 1906, Band lix, p. 29.

30 drops of Reuter's stain (Grubler), or (b) 10 drops Giemsa in 10 c.c. distilled water; (4) wash with distilled water; (5) cover and seal with vaselin. These preparations last for several days. From his studies of sputum he concludes that the chief constituent of spirals is eosinophiles, the mucus serving only as binding material for those cells. He describes three types of spiral structures: (1) Broad spirals without central threads; (2) typical spirals with central threads; (3) isolated central threads. Only the last mentioned, in addition to rudimentary spirals, show a simple structure, and consist solely of thin mucin threads. He says one cannot hold Curschmann's spirals as specific for bronchial asthma, but only as a bronchial secretion, out of which, during attacks, the spirals form, the latter consisting of mucus and enormous quantities of eosinophile cells. None of the eight reported cases furnishes confirmation of this view.

In this discussion of the site of the lesion and of the spirals in bronchial asthma, the observations of Riehl<sup>20</sup> deserve a place. He reports sputum studies from four cases—two in males, two in females—in which the spirals differed considerably from those in ordinary cases, and which suggest an unusual location of the disease process, although not necessarily a difference in the process itself. In the sputum of each patient were "giant" spirals ranging from 6 to 24 cm. in length, and in some instances attaining a breadth of 3 to 3.5 cm. Microscopically no spirals of the ordinary size were found. Charcot-Leyden crystals were found in none of the specimens. Riehl can account for the large spirals only by assuming that they were formed in bronchi of the first order, instead of in the smaller tubes. The clinical course supported this assumption, there being in general a lack of considerable dyspnoea and of physical phenomena in the air passages. There was severe dyspnoea while the spirals were being expectorated, as was not surprising in the presence of masses capable of obstructing large bronchi. The patients were usually ill several days before cough and expectoration began. Riehl regards the cases as illustrating a variant of bronchial asthma, in which only isolated larger bronchial branches were affected—an "isolated" rather than "diffuse" asthma. None of the cases coming to autopsy has been of this type.

Schmidt is correct in stating that *it is impossible from anatomical findings alone to construct a picture of the mode of origin of spirals*. According to his view the power that produces the central threads from mucous masses must have its application within the bronchial lumen, and, corresponding to the gradual formation of spirals, its action cannot be narrowed to any fixed point. He believes this producing power can be no other than the rotary movement of the air which is forced through the tough mucus and which acts upon



that material during its entire passage from the finer to the larger bronchi.

As a final statement regarding the nature of spirals is to be noted the opinion of Kaufmann. He states that for the production of spirals, which consist of mucus, there is requisite the presence in the bronchi of a scanty, tough, mucous secretion which, by violent respiratory efforts, by the associated pressure and the convulsive movements, possibly also by contraction of the bronchi themselves, is formed, and turned and driven forward. In this process the central part of the mucous string becomes so dense that it appears as a shiny, homogeneous thread (which, however, is no peculiar structure in itself), surrounded by the looser spiral mucous mantel. He states without comment that Schmidt regards this mucus as a special secretion of the finest bronchi, which possess no mucous glands, and that Fraenkel holds it to be the cylindrical epithelial cells of the finer bronchi which have undergone mucous degeneration.

*The origin and significance of the eosinophile cells and the crystals often found in the sputum and the pulmonary tissues in cases of bronchial asthma is a widely discussed and still unsettled question.* Both are found in other affections, hence neither is specific for asthma. Literature on the former subject is so extensive and so connected with the subject of eosinophilia in general that it would lead too far afield to consider it here *in extenso*. It will not be amiss however, to refer to a few of the earlier and some of the more recent opinions regarding the nature of eosinophiles, especially in the respiratory tract, and their connection if any, with Charcot-Leyden crystals. Their possible etiological relation to Curschmann's spirals has already been mentioned.

Lewy<sup>21</sup> concludes that these crystals, as well as the spirals, are only a consequence of the desquamating catarrh in the bronchi, and are not specific for a special clinical disease picture. Later<sup>22</sup> he states there is a relation between eosinophile cells and the crystals, but considers it impossible to say just what this relation is. Weiss<sup>23</sup> discusses a moot question—the local formation of eosinophiles. He found those cells in the sputum from cases of chronic bronchitis with acute exacerbation and of pulmonary tuberculosis, in addition to that of bronchial asthma. In the last two he states specifically there was no increase of eosinophiles in the blood. He believes they do not come from that source, and that they are undoubtedly locally formed. That they are an etiological factor in bronchial asthma he regards as improbable. Aronson and Philip<sup>24</sup> found that in the sputum of a nine-year-old asthmatic patient nearly two-thirds of the whole number of cells were eosinophiles. A noteworthy point was that a large number of these cells were mononuclear, a type

<sup>21</sup> Ztschr. f. klin. Med., 1885, Band ix, p. 522.

<sup>22</sup> Ibid., 1900, Band ix, p. 59.

<sup>23</sup> Deut. med. Woch., 1892, Nr. 3, p. 48.

<sup>24</sup> Wien. med. Presse, 1891, Nrs. 41-44.

seldom found in the blood. They, however, found that the eosinophiles in this patient's blood ranged from 15 to 17 per cent. of all the leukocytes. Teichmüller<sup>26</sup> found eosinophile cells in the entire respiratory tract of guinea-pigs, cows, sheep, swine, horses, and rabbits. He believes one may well regard the lungs and bronchi as local forming places for these cells. Later<sup>26</sup> he describes cases of "eosinophile bronchitis," specially characterized by the great number of eosinophile cells in the sputum.

Fuchs<sup>27</sup> concludes that eosinophile cells have no one method of origin. They can arise from neutrophile granules, and also, by phagocytosis, from metamorphosed red cells. Their origin is restricted to no one place, and they may arise in all tissues and in all organs. The eosinophiles of sputum probably originate in the respiratory tract. They are of no differential diagnostic value in bronchial asthma, as they may appear in all diseases of the respiratory tract unaccompanied by fever. Stschastnyi<sup>28</sup> reaches similar conclusions regarding eosinophiles being formed through the phagocytosis by mesenchyma cells of fragments of hemolyzed erythrocytes. Consequently, eosinophiles can be formed wherever hemolytic and phagocytic processes are active; usually the principal sites are the bone-marrow, lymph nodes, spleen, and lungs. The appearance of eosinophiles in asthma, he believes, is explained by the observation of an unusual collection of those cells in the region of the bronchi after the injection into the blood of hemolytic serum. In asthma, with the observed vasomotor disturbances and hyperemia of the bronchial mucous membrane, there are furnished conditions favorable to the destruction of red cells and their ingestion by mesenchyma cells.

Pröscher<sup>29</sup> says we must accept that with the greatest probability the eosinophiles in bronchial asthma are locally formed. Though for some years believed to occur, the direct transformation from tissue cells to eosinophiles had not hitherto been observed. He details experiments made upon guinea-pigs which he regards as furnishing positive proof of such transformation, and hence of the local formation of eosinophiles, thus giving a sound experimental basis to previous theories. He employed intraperitoneal injections of non-absorbable teniotoxin, this producing a rich eosinophile exudate, in which could be clearly traced the transformation from eosinophilic granulated endothelial cells to mononuclear eosinophilic leukocytes. Pröscher holds that eosinophile granules are identical with hemoglobin. Mosny and Harvier<sup>30</sup> report what they believe to be the first recorded case of local meningeal eosinophilia, and

<sup>26</sup> Deut. Archiv f. klin. Med., 1898, Band ix, p. 576.

<sup>27</sup> Ibid., lxiii, p. 444.

<sup>27</sup> Ibid., 1899, Band lxiii, p. 427.

<sup>28</sup> Beiträge z. path. Anat. u. allg. Path., 1905, Band xxxviii, p. 456.

<sup>29</sup> Folia Hematologica, 1905, Band ii, p. 543.

<sup>30</sup> Arch. de méd. exp. et d'anat. path., 1907, No. 3, p. 273.

regard it as proving incontestably that eosinophiles originate from lymphocytes. The patient was a man aged twenty-six years, suffering from syphilitic meningo-encephalitis. In the meningeal exudate they traced all forms of cells between the lymphocyte, or original cell, and the polynuclear eosinophile. The patient recovered; hence their studies were limited to the cerebrospinal fluid and the blood. The latter never contained more than 1 per cent. of eosinophiles. Brown<sup>31</sup> considers it probable that in trichinosis eosinophiles arise from degenerated muscle cells.

In opposition to these opinions regarding the local formation of eosinophiles, a number of writers favor the view that those cells found in bronchial asthma and in other affections arise in the hematopoietic organs, or at least are not locally formed. Müller<sup>32</sup> regards the Charcot-Leyden crystals as the primary occurrence, the eosinophiles as a result. The former are the crystallization product of a substance which possesses a positive chemiotaxis for eosinophiles. Wolff<sup>33</sup> studied the blood of a patient during and between attacks of bronchitis and asthma. The eosinophiles ranged from 6 to 14 per cent., and were little changed during the attacks. In another case of asthma, 7 per cent. of the cells in the sputum were eosinophiles, while those cells in the blood varied between 15 and 39 per cent. Heineke and Deutschmann<sup>34</sup> report a case believed to be unique. A patient who had had bronchial asthma for four years showed, at the beginning of attacks, a diminution of the eosinophiles in the blood, from 2.1 per cent. to 0.4 or 0.6 per cent., and then later, corresponding to the appearance of those cells in the sputum, an increase up to 10 per cent. They believe it impossible that the enormous number of eosinophile cells in the sputum could have come from a source other than the blood; only this supposition can explain to them the rapid diminution of eosinophiles in the blood at first, and then their increase as the bone-marrow, on the second day, began to react to the specific irritation. Recently v. Hoesslin<sup>35</sup> has reported a case in which the eosinophiles showed changes similar to those just described. The eosinophiles and lymphocytes both diminished during the attacks of asthma, the polynuclears increasing. As the attacks waned there was a rapid increase of the two first forms and sinking of the polynuclears below normal. The eosinophiles during these periods reached 10 per cent. Aubertin and Ambard<sup>36</sup> performed experiments on dogs to determine if eosinophiles, especially in the alimentary tract, are formed *in situ* or in the blood. After injection of secretin they found that eosinophilia of the blood (9 per cent., of which 1 per cent. were mono-

<sup>31</sup> Jour. Exp. Med., 1898, vol. iii, p. 315.

<sup>32</sup> Centralbl. f. allg. Path., 1893, Band iv, p. 529.

<sup>33</sup> Beiträge z. path. Anat. u. allg. Path., 1900, Band xxviii, p. 150.

<sup>34</sup> Münch. med. Woch., 1906, Nr. 17, p. 797.

<sup>35</sup> Ibid., 1907, Nr. 44, p. 2183.

<sup>36</sup> Compt.-rendus Soc. de Biol., 1907, t. lxxi, p. 263.

nuclear) persisted for three months and without the presence of eosinophiles in the intestinal wall, where they appear in large numbers during digestion, unaccompanied by any appreciable increase in the blood. In addition to the hemic eosinophilia, the spleen was enlarged and showed marked myeloid transformation, containing large numbers of myelocytes and polynuclear eosinophiles. This, in connection with other similar studies, inclines these writers to believe that all eosinophiles are formed in the marrow or spleen.

Reference to the accompanying table will show that in the reported cases with autopsy the findings in regard to eosinophile cells have been variable. Not only is this true of their presence and numbers in the bronchial lumina and walls and in the alveoli, but also of their type. In one of Fraenkel's cases, for example, they were largely mononuclear; in mine, all polynuclear. Equally dissimilar findings have been recorded in sputum studies. I cannot see that these eight cases throw the least light upon the origin and significance of these cells in bronchial asthma. That they are not specific for this affection has been abundantly shown, although Predtetschensky is inclined to regard their enormous numbers as savoring of specificity. If some of the writers here quoted, Stschastnyi in particular, are correct in their theories of the local origin of eosinophiles, the possibility is suggested of finding those cells in the pulmonary tissues in cases of local or general chronic circulatory disturbance in the lungs, especially when accompanied by apparent interference with the vagi. It may be, however, that in most chronic affections phagocytosis is in abeyance regardless of the increased hemolysis accompanying such conditions. The study of large series of lungs exhibiting varied lesions should throw some light upon this question. Such studies now being made by me have already led to interesting results, regarding which I hope to make a further communication.

The so-called Charcot-Leyden crystals found in many cases of bronchial asthma are likewise not characteristic of any special disease, being found in the blood, spleen, and bone-marrow in cases of leukemia, in nasal polyps and other tumors, in normal marrow, pus, feces in cases of helminthiasis, and in other tissues under certain conditions. They also appear, but less often than in asthma, in other pulmonary affections, as emphysema, bronchitis, and tuberculosis. Their origin and significance are uncertain. Hyneku<sup>77</sup> believes they arise principally in eosinophile leukocytes through degeneration of their spongioplasm. In this view he is supported by Predtetschensky, and Kaufmann regards it as a possibility. Müller's opinion, that they are the crystallization product of a substance in the tissues, has already been cited.

<sup>77</sup> Quoted in Schmidt's *Jahrbücher*, 1907, Band ccxlv, p. 187.

*In conclusion, it must be said that the pathological anatomy of bronchial asthma, as revealed in these eight cases, constitutes no exposition of the cause of the disease.* The findings furnish a fairly satisfactory explanation of some of the clinical features, especially distention of the lungs and dyspnoea, and locates the source of some of the constituents of the sputum. Why those substances are formed is not clear. Further, and this point is of paramount interest, the histology furnishes no explanation of why the formation of such substances in the lungs in these cases gave rise to the clinical phenomena designated as bronchial asthma, while in other cases, with the presence of essentially identical materials, that symptom complex is lacking. The mucus, bronchial epithelium, leukocytes, eosinophile cells, Charcot-Leyden crystals, and spirals discharged from or found in the respiratory tract in cases not clinically bronchial asthma, are, it is true, not invariable in quality and quantity, but neither are they in asthma itself. We are consequently forced to regard the latter affection as the result of a cause as yet undemonstrable by studies of the lungs of these subjects. Inquiries as to the location and nature of this cause have led clinicians to advance the theories mentioned in the introductory paragraphs. Further discussion of these theories is beyond the scope of this paper, which deals only with the actual pathological anatomy of the disease in question.

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### HENRY GRAY, ANATOMIST: AN APPRECIATION.

BY FRANK K. BOLAND, M.D.,

OF ATLANTA, GEORGIA.

IN reading a little book entitled *The World's Anatomists*, and written in 1905 by Dr. G. W. H. Kemper, I was struck by the fact that the only mention of Henry Gray is the date of his birth and death, and the statement that he was an Englishman and the author of a text-book on anatomy. This seemed but meagre notice, indeed, of a man whom medical students and physicians for a half century have been accustomed to think of as a most distinguished anatomist; and I resolved to find out more about him if I could. Surely a man must have been very little short of a genius to have written in his time the book he did at the age of thirty-one years. Today most of us have only begun to live at thirty-one; but Gray had accomplished more at that age than the great majority of us can hope to accomplish if we live twice as long.

Although dead less than fifty years, so little information concerning Gray's life has been published that an air of mystery seems to have

developed about the young man. This is accounted for in part by his early death and by the fact that he left no direct descendants to record the particulars of his career. These circumstances made the search for data an especially interesting, although difficult, task. I wished to know something of Henry Gray's life and to ascertain how much of Gray is Gray. The year 1858 was too late for one to make any great discoveries in anatomy, but a method of presenting the subject could be original, as could descriptive names and expressions.

The facts here given come through the courtesy of Mr. Robert Harrison, assistant secretary of the Royal Society, of which Gray was a member, and Mr. E. I. Spriggs, dean of the St. George's Hospital Medical School, Gray's alma mater, who secured for me the aid of Mr. C. T. Dent, the senior surgeon, to whom I am indebted more than to any one else. Mr. Dent gathered information from various records, and from interviews with Mrs. Stonhill, one of the two surviving relatives of Henry Gray, from Mr. Pickering Pick, one of the editors of the *Anatomy*, and from others of the few living contemporaries of the author. Without the assistance of Mr. Dent, this sketch would have lacked much of its detail.

Henry Gray was born in 1827, in London, probably, although it is not stated positively. His father was private messenger to George IV and William IV. He had one sister, who died at the age of twenty-one years, and two brothers. One brother died young; the other was Thomas William Gray, who had two daughters, one of whom is Mrs. Stonhill. This lady can give but little information about her uncle, so that where he passed his boyhood and where he received his preliminary education is not known. The date of his father's death is not on record, but young Gray does not seem to have been beset with the financial obstacles which so often handicap men of talent. His student and professional course to success was uninterrupted. There are now but few survivors who were his contemporaries at St. George's Hospital, and they appear to know nothing of his career previous to his entrance as a student.

Gray's signature appears on the pupil's book at St. George's Hospital, as entering on May 6, 1845, as a "perpetual student." This term, although probably customary, serves to illustrate the earnestness with which the eighteen-year-old youth took up his chosen work. At this time there was no medical school within the hospital precincts, but some rooms had been rented in Kinnerton Street, not far from the hospital, and it was there that the teaching in anatomy, physiology, and the other rudimentary branches was done. The lectures on medicine, surgery, and the clinical part of the curriculum were given at the hospital. Mr. Henry Charles Johnson, who was assistant surgeon to the hospital from 1843 to 1853, is believed to have been the lecturer on anatomy when Gray matriculated.

There is no evidence to support the absurd story that Gray was a poor student and failed in some of his examinations; the facts tend to prove the very opposite. In 1848, at the age of twenty-one years, he was awarded the Triennial Prize of the Royal College of Surgeons of England for a paper on "The Origin, Connection, and Distribution of the Nerves of the Human Eye and its Appendages, Illustrated by Comparative Dissections of the Eye in the Other Vertebrate Animals." Although this prize was first instituted in 1822, it has had only eight recipients.

Young Gray assuredly possessed great talent and untiring energy. The opinion of all those who remember him agrees in describing him as a most laborious and methodical worker, and one who learned his anatomy by the tedious but invaluable plan of making his dissections himself. Judging from the results he obtained, he had no time for anything but his work.

In June, 1850, he was appointed house surgeon to St. George's Hospital, which position he held for the customary twelve months. On June 3, 1852, he received the distinction of being elected a Fellow of the Royal Society at the remarkably early age of twenty-five years. His hospital record and his activities in original research must have been highly esteemed to have secured him such honor. It has been supposed that he obtained the title largely through the influence of Sir Benjamin Brodie, who became president of the Royal Society in 1858. But Brodie himself was only elected a member of the Society in 1849, and does not appear even to have supported the candidature of Gray, although no doubt he took a warm interest at that time in so promising a pupil of the hospital. Brodie ceased to be surgeon to St. George's Hospital in 1840, but continued his active interest in the medical school, and, indeed, advanced the capital for the purchase of the lease of the buildings in Kinnerton Street.

Gray won the Astley Cooper Prize of three hundred guineas in 1853 for his dissertation on "The Structure and Use of the Spleen," a work which ranks next in importance to his *Anatomy*. This prize is awarded triennially, and is open to the world, students of Guy's Hospital alone being debarred from competing. Other papers which Gray had written up to this time were: In 1850, "On the Development of the Retina and Optic Nerve, and of the Membranous Labyrinth and Auditory Nerve;" in 1852, "On the Development of the Ductless Glands in the Chick;" and in 1853, "An Account of a Dissection of an Ovarian Cyst which Contained Brain."

From 1853 to 1858 he was lecturer on anatomy at St. George's Hospital. It is also recorded that he was surgical curator of the Pathological Museum during this period. No doubt his services as demonstrator of anatomy were very much in demand, for he had established a considerable reputation while a student. His time

must have been given very largely to the dissecting room, and we learn nothing of his experience in clinical work.

Gray now devoted his energies to the preparation of the work by which he is really known, the masterpiece, *Anatomy, Descriptive and Surgical*. Since this work is the only one of its kind which has come down to us from this time, the idea exists that no good books on the subject had been written before. Nothing could be more erroneous. Many excellent anatomies were in common use at the time Gray's made its appearance, and the new work was pitted against keen competition. Quain and Sharpey's *Anatomy* was probably the most popular book, although others, such as Wilson's and Winslow's, and the translations of the French writers, Cruveilhier, Bichat, and Cloquet, had strong following.

Gray undoubtedly felt that there was room for improvement in these treatises, particularly in the matter of arrangement and illustrations. He had a good conception of the principles of pedagogy, and desired, in so far as he could, to smooth for his students the hard road to anatomical knowledge. A comparison of Gray's work with that of his predecessors shows that he achieved his purpose in an admirable manner. He was not the Father of Anatomy, and it was not the presentation of any new anatomical discoveries, but the clearer and more systematic presentation of old ones, backed strongly by unparalleled drawings, which secured for his book its phenomenal success.

To Dr. H. Vandyke Carter, who made the drawings, a large part of the credit for the success of the work must be given. Gray, in the preface to the first edition, which is dated August, 1858, "gratefully acknowledges the great services he has derived, in the execution of this work, from the assistance of his friend, Dr. H. V. Carter, late demonstrator of anatomy at St. George's Hospital. All the drawings from which the engravings were made were executed by him. In the majority of cases, they have been copied from, or corrected by, recent dissections, made jointly by the author and Dr. Carter." In this preface, "the author also has to thank his friend, Mr. T. Holmes, for the able assistance afforded him in correcting the proof sheets in their passage through the press." According to Mr. Dent, the assistance that Mr. Timothy Holmes afforded was considerably more than might appear from this acknowledgment. Mr. Holmes had the literary gift developed to a very high degree. Mr. Dent thinks that the literary excellence of the first edition of the anatomy was mainly due to Mr. Holmes' suggestions, but this does not detract at all from the scientific value of Gray's work as an anatomist, or from the skill shown in the arrangement of the text.

The first edition was published by John W. Parker & Son in 1858, and was the only edition that Gray ever saw. The book was a success from the first. Such clear treatment of descriptive anatomy



had not been known before, and there has been but small improvement, except for additions, made in it since. The introduction of the remarks on surgical anatomy was the first ever attempted by an English author, and proved to be a popular feature.

The cuts far exceeded in number and excelled in accuracy and vividness any which had appeared previously. It is astonishing to see how many of these drawings are in the *Gray* of today. Indeed, very few of them have been discarded, wherein good judgment has been displayed, because as diagrammatic representations they would be hard to surpass, and such representations are more readily grasped by the student than any other.

Nevertheless, the critics were by no means unanimous in their praise. The *Lancet*, in its review, spoke in the most favorable terms, but the *Medical Times*, which was then the chief rival of the *Lancet*, took an altogether different view, its reviewer indulging in what was then known as a "slashing criticism." Gray was accused of freely borrowing from Quain and Sharpey's *Anatomy*. This work was the text-book then commonly in use, and the student was likely to saturate himself with it as succeeding generations have saturated themselves with Gray's *Anatomy*.

There is no doubt that many passages could be cited in which the phraseology very closely resembled that of Quain and Sharpey. But we know, without question, that most of Henry Gray's work was done from actual dissections. After all, anatomical descriptions cannot vary greatly, and it is more than probable that in the passages quoted by the critics, Gray was borrowing quite unconsciously when he described the dissections that were actually before his eyes.

Parker & Son's business was bought up by Messrs. Longmans, and the second and all succeeding English editions of Gray, now numbering sixteen, were published by the latter firm. This was a potential factor in the perpetuation of the work, since this firm has long been known as one of the most enterprising of publishers.

Even prior, however, to Longmans' purchase, the firm of Blanchard & Lea, now Lea & Febiger, of Philadelphia, had arranged with Parker & Son for the publication of Gray's *Anatomy* in this country. As Longmans' purchase was subsequent and subject to the arrangement of Parker & Son with Lea & Blanchard and their successors, the longest connection between the book and any of its publishers enures to the credit of America. During this long period the firms of Longmans and of Lea & Blanchard and their successors have cordially coöperated for the benefit of the book and its readers. It is not too much to say that the services of many of the most distinguished anatomists of the English-speaking race on both sides of the Atlantic have been enlisted in successive revisions.

Mr. Holmes became the editor after Gray's death, and subsequently Mr. Pick, both of whom were friends of the author and lecturers on anatomy and surgeons to St. George's Hospital. The

book has been doubled in size, and altered by English and American editors, but much of the original matter can be distinguished, especially in the arrangement. For example, the method of showing the relations of arteries by the ring with the adjacent structures grouped around it, so simple and yet so helpful, still remains as in the first edition.

In 1861 Gray was a candidate for the post of assistant surgeon to St. George's Hospital, two vacancies having at that time occurred. He would certainly have been elected, but unhappily was attacked by confluent smallpox, which he contracted while looking after his nephew, who had fallen a victim to the same disease. After a very short illness, Henry Gray died on June 13, 1861, at the age of thirty-four years.

He was at work on the second edition of his book at the time of his death, and had made good progress with a work on *Tumors*. The manuscript of this cannot now be found, and no part of it was ever published. Before his death Gray had been made a Fellow of the Royal College of Surgeons by examination, and surgeon to St. James' Infirmary.

These are the facts concerning Henry Gray's life as I have been able to gather them. They are no doubt genuine, but I trust their publication will be the means of bringing to light much more about such an inspiring character. I much regret that I could not learn more of the personal side of his character. His portrait shows the face of a man who might have been a great artist; the forehead is high and broad, the eyes are set widely apart, and the chin is powerful. Altogether his appearance commands attention, and we know at a glance that he was no ordinary person.

There is nothing recorded about his ability as a diagnostician or operator. The plan of his professional career, which is worthy of emulation, seems to have been first to ground himself thoroughly in the fundamental branches of anatomy and pathology, after which he would be equipped for the best possible work in the field of practical surgery.

He was about to quit the dissecting room for the operating amphitheatre when his life was brought to a sudden close. Sir Benjamin Brodie must have had this in mind when writing the letter reproduced herewith.

Of the estimation in which Gray was held at the time of his death, this letter furnishes eloquent testimony. Sir Benjamin Brodie was Sergeant-surgeon to the Queen, and one of the most distinguished of English surgeons, and it was to him that Gray dedicated his *Anatomy*. Brodie was nearly blind at this time, and very seldom wrote; indeed, this letter was probably the last that he ever put on paper. The latter was addressed to Mr. Charles Hawkins, one of the governors of St. George's Hospital, and his literary executor. The lady therein referred to, whose name is illegible, must have been

the one to whom Gray is said to have been engaged at the time of his lamented decease. A fac simile in my possession, which is difficult to decipher, reads as follows:

JUNE 15, 1861.

MY DEAR SIR: I am much grieved about poor Gray. His death, just as he was on the point of obtaining the reward of his labors, is a sad event indeed. If you have any means of doing so, I wish that you would express to Miss —— how truly I sympathize with her in her affliction. Gray is a great loss to the hospital and the school. Who is there to take his place?

Yours ever truly

B. C. BRODIE.

From this brief study of the life of Henry Gray, which was undertaken with the purpose of determining his true place in medical history, I am happy to conclude that he is entitled to the fame that is his. Although confessedly the glamour of renown has been augmented by clever illustrators, able editors, and progressive publishers, yet we could not fairly snatch away a single ray when we consider the part he played in the time allotted him. These factors are always instrumental in the success of such work.

Gray's genius, like that of many others, consisted of hard work and singleness of purpose; could he have lived long enough to carry this with his spirit of investigation farther into medical science, it is reasonable to believe that he would have left a name as great as surgeon as it is as anatomist and teacher.

## REVIEWS.

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1. LE CANCER: PROPHYLAXIE, ETIOLOGIE, TRAITEMENT. By C. SOBRE-CASAS, Médecin à l'Hôpital Rawson (Buenos Ayres). Pp. 219. Paris: G. Steinheil, 1908.
2. CANCER: RELIEF OF PAIN AND POSSIBLE CURE. By SKENE KEITH and GEORGE E. KEITH, authors of a *Text-book of Abdominal Surgery*, etc. Pp. 155. New York: The Macmillan Co., 1908.
3. THE CONQUEST OF CANCER. By C. W. SALEEBY, M.D., Pp. 361. New York: Frederick A. Stokes & Co., 1907.

THE study of cancer is no man's field. That the whole medical world is engaged upon the problem is almost a platitude, for its verity; and the multitudinous publications, varying from profound to vagaries, necessarily include observations and speculations dealing with the most varied aspects of the question. That eventually there must be a conclusive answer to the great question as to the nature and origin of cancer, and that this must lead to a more nearly perfect idea of its treatment, cannot be doubted; and there is no telling whether success will come by the systematic elaboration of any one of the existing theories or whether it will be brilliantly exhibited by new lines of inquiry. It is safe to say, at least, that at the present no conscientious effort along any reasonable line can be disregarded as improper. All of three books herewith reviewed, therefore, are worth consideration, although they differ most widely in their attitudes and in the impressions which they leave upon the professional reader.

Dr. Sobre-Casas' brochure attempts in systematic fashion to review the general field of the present aspect of the subject, without any pretence toward elucidation of the obscure problems of the pathology of cancer or of advancing any specific measures for its cure, but rather of condensing the more important contributions upon the etiology of the malignant tumors and what has been written concerning prophylaxis and treatment. It thus seeks to give a convenient basis, a sort of stock-taking, to facilitate comparison and permit of more intelligent procedure into further study. After a brief introductory chapter upon prophylaxis, in which a plea is made for education of the public to the danger of postponing proper examination

of suspicious growths, the author outlines the work in Europe, this country, and his own as far as organization of systematic studies and provision of special hospitals and laboratories for the care and investigation of cancer are concerned. A cursory review of the various non-parasitic theories, and a somewhat fuller consideration of problems relating to a possible parasitic origin (with more particular details as to evidence of spontaneous inoculations and experimental transmissions) are succeeded by a brief reference to various causes which apparently are contributory to the development of cancer, as age, profession, traumatism and chronic irritations, heredity, arthritism, alimentation, arsenic, the influence of races, and the disproportionate frequency of cancer in certain localities. A suggestive but very brief part of this chapter deals with the actual physiological state of the host of advanced cancer, notably the atrophic condition of the heart and other organs and the alterations of the blood. The chapter upon treatment in turn takes up the surgical means and the results of surgical measures in cases of cancer in various parts of the body, a long list of physical and chemical measures and agents which have been advocated at one time or another and their results, a discussion of the ten or more serum methods which have been advocated in the hope of specific results, together with a brief consideration of palliative means. A short chapter upon general hygiene in cancer and a few pages of summation are succeeded by a biographical reference list fairly representative of European writers.

M. Sobre-Casas is optimistic as to the future of the work against cancer. The volume is the *resume* of his studies made in the course of a mission in Europe authorized by the Argentine Government, with the purpose of directing further work in Argentine, where, as elsewhere, the proportionate number of cancerous cases is on the increase. While he adopts the aphorism "early diagnosis, immediate operation," he looks forward to the attainment of a specific means of treatment, and clearly inclines to some form of parasitism as the causative agent of malignant tumors. The book, however, is a very fair and a reasonably conservative, and, at the same time, a widely inclusive, *resume* of the subject. It is valuable for the purpose set the author, and reflects credit upon him in the performance of his official mission. There are numerous inaccuracies in spelling and some in typography, which mar the general tone of the volume.

The Keiths' little volume, largely occupied with the histories of cases of cancer illustrative of the effects of a method of treatment advocated by the authors, has as its prime purpose the establishment of the belief indicated in its title. The procedure in question is nowise to be substituted for the early surgical ablation of cancerous tumors, but is urged in those instances in which operative measures cannot for one reason or other be undertaken, and as an adjuvant

when this is desirable. The authors have no theories to advance, and have little that is good to say of specific medications. Their method consists simply in the employment of a combination of arsenic and iodine, both long known and of some repute as medicinal agencies in the treatment of malignant disease. Their combination is an emulsion containing iodipin, arsenate of iron, cacodylate of iron, and cinnamate of sodium, mixed according to directions stated in the volume, but not so clearly as might be wished. It is administered hypodermically in the arm, buttocks, abdominal wall, or other part as desired, and there is some variation among individual cases as to the degree of tolerance found and the resultant value. The authors claim from the use of the remedy, now employed for some years by them, a distinct prolongation of life, general physical improvement, and a very decided relief from pain, particularly when this symptom is in the cancer and due actually to it, rather than to pressure by the tumor mass or to ulceration or other complication. They believe that there is less tendency toward recurrence when the combined drugs mentioned are employed after operation, and they express a hope, which, however, they are unwilling to rely upon, that in selected cases it may be curative. Two-thirds of the volume is occupied by case histories of cancer and a few of sarcoma illustrative of the arguments of the writers.

It is probably as much a matter of habit among our British brethren as one of taste whether such a communication be accorded the dignity of a separate volume or take its chances as a journal article. Certainly the former offers the advantages of a greater exhibition of details of corroboration, and, if the measure advocated reach in other hands the same measure of beneficence as in the experience of the authors, no one may begrudge it or them the distinction afforded the subject by the neat presentation the publishers have given it.

Saleeby's is a book that the reviewer is disposed to believe would not take its present title, or make as insistent demands for acceptance, were it to be undertaken at the present moment. It is most attractively written, and is singularly persuasive in its arguments and verbiage, and is withal very suggestive and valuable from its sidelights upon the subject. But in its main purpose, the advocacy of an idea, it is today an unhappy outrunner of a theory which is unproved and but poorly sustained and lags behind this defending and promulgating volume. Dr. Saleeby seeks in his book to prove as of specific and general application among the malignant growths the idea of Professor Beard—and succeeds to his own satisfaction; and it is more the pity that the world's experience has not better fulfilled his expectations in the use of the specific medication for cancer which the theory is supposed to indicate. That there have been instances of cancerous growths in which the use of trypsin has been followed by cure is undoubted; but so, too, there have been

recoveries after the use of forty different other agencies which, superficially at least, have even less claims to be curative than has the pancreatic secretion. That there have been failures from the use of trypsin, surely, in equal measure to the proportion of failures from the multitude of other cures, the days and months are constantly giving evidence. And it is essentially in this point that Saleeby has placed his justification, that the logical and presumably infallible remedy has been found; in which, therefore, he has also met his undoing. It would be an impertinence, even now after the failure of the trypsin treatment to establish its inherent correctness, to criticise in the same spirit and with the same lack of hesitancy the theory of the trophoblastic origin of tumors. In this Professor Beard is not contradicted, and the theory must await with the other theories, whether developmental, parasitic, or what-not, for a final answer, which does not as yet prevail. That trophoblasts, undifferentiated developmental cells of the segmentation body, are not completely utilized in the formation of the economy is assured; that some of these may be included in the forming embryo may likewise be accepted; that these disappear coincidentally with the formation of the pancreas (which, for that matter, nearly agrees with the formation of the hepatic diverticula as well) is a contribution which Beard makes, and is of necessity a matter of undoubted interest, but of unproved relation with the pancreas. That there are types of growth which singularly suit our ideas of the behavior of trophoblastic development as the various teratomas is true; and that there is a nice gradation possible to be made out (although it may be quite artificial and forced in one sense) between these and the ordinary types of malignant growths is also true; and, given a cell capable of indefinite proliferation and variable or even multiple differentiation, one can only accept the theoretical origin of a given type of cancer from it on the ground that differentiation of the cells does occur with proliferation. But in such case, in order to explain the uniformity of histology of primary cancers in different structures, one must aver an adapting influence of these parts upon the growing tumor cells; and when this is said, one is face to face with the further problem why the tissues about secondary tumors do not with equal power exert their power of adaptation upon the secondary foci. And inasmuch as the malignant teratomatous types give metastases which conform to their multiform progenitors, why do not the tissue in which they are lodged interfere with their polymorphous character and impose a specific type upon them? It is particularly on this point that Beard's theory of tumor formation differs from Cohnheim's embryoblastic theory, that is, in the question of the stage of differentiation of the tumor anlage; Beard's idea demands a cell as yet undifferentiated but capable of differentiation, Cohnheim's accepting the actual differentiation into cells of definite type in the anlage. In neither is it a vital objection that tumors are not of more

common occurrence in early than in later life; yet it is not unfair to regard this as a weakness of both theories from our present standpoint. If, as Cohnheim has indicated, according as the embryonal anlage of a tumor represents an early or a late separation or cellular excess, there should be a rapid or more slow rate of growth to characterize the tumors; one is given further reason for question why, if tumors arise from included trophoblasts with an undoubted inherent potentiality of very rapid proliferation, do these neoplasms show such variability in rate of growth; why are they not all of highly rapid growth? If it be the pancreas which destroys these aberrant trophoblastic cells in the economy and prevents their growth into tumors, why should there be no plainer relation between pancreatic failures of one sort or another and the occurrence of malignant disease? Why should there be cancer in the pancreas itself?

Such questions and objections are, to the reviewer's mind, entirely fair, and such matters and many more of the same type, some perhaps even more insistently, must be satisfied before final acceptance of the theory as more than a pure hypothesis for the general group of the malignant growths. But it must at once be acknowledged that, so far as the part of the trophoblast being the basis of origin is concerned, and shorn of the pancreatic relation and the insistence that trypsin is the necessary cure-all of cancers, there are practically as many points of favor of the theory as of any of the developmental theories. That these tumors are not the result of parasitism, but are themselves the parasites, has strong reason for consideration, and that thus in a modified form, and perhaps limited to certain special types of malignant tumors, the theory may eventually come into definite favor cannot be gainsaid. The idea of chemical relations which is embodied in the supposition that the pancreas is the cause of the disappearance of the trophoblast in the embryo, and that it, therefore, is responsible for permitting the tumor growth by some kind of inefficiency in later life, is an application of the broad theory of hormones to this particular subject; and this, too, is worthy the most careful and prolonged inquiry. But that the pancreas is necessarily the point of origin of such chemical restrainers or chemical stimulants to growth entirely lacks proof. That the corpus luteum chemically stimulates the development of decidual cells, and may be potent in production of deciduomas, may be accepted as proved; and the principle probably has a wide range of applicability. Experience with pancreatic extracts in cancer gives but little reason to believe this organ either energizes or restrains proliferation of any of the tissues or cells liable to develop into cancer; but somewhere in the body there may well be structures which are responsible in this very fashion.

Such considerations, it seems to the reviewer, are more to the point in the consideration of this book than a detailed discussion of the book itself. The attitude of the author as an enthusiast, his



unwarranted and pettish criticism of the "authorities that be" for not seeing the same things in the same light as he does himself, his advocacy as a fact of a theory in its entirety which has not any more grounds for acceptance of its best parts than other existing theories, and plenty of contradiction in application of its practical phases—these are the unfortunate sides of the making of the book. That it is a well-made book, that it places in the most logical and appealing way the subject-matter before the reader, that it is suited, as the author intends, for the ready perusal and easy understanding by a wide group of the public as well as medical readers, must be acknowledged.

For the technique of the argument and presentation the author is to be complimented; for the insufficiency of his subject-matter and the failure of its high claims he is to be commiserated; but for his injudicious haste and misleading claims in the attempt to establish an enticing but untried theory as a working reality, there can be little but reprimand.

A. J. S.

DIAGNOSTICS OF THE DISEASES OF CHILDREN. By LE GRAND KERR, M.D., Professor of the Diseases of Children in the Brooklyn Postgraduate Medical School. Pp. 542; illustrated. Philadelphia and London: W. B. Saunders Company, 1907.

In this recent contribution to the already well covered field of pediatric literature, Dr. Kerr has satisfied a long-felt need. Students of pediatrics have searched in vain through the larger text-books on diagnosis for a satisfactory consideration of the subject as applied to diseased conditions in childhood. Whatever references may be found are either sketchy or wholly inadequate. Dr. Kerr's book, therefore, may serve not only as a supplement to previous works on general diagnosis, but also as a complement to the comprehensive text-books on pediatrics which have appeared within the last few years. A careful perusal of the book convinces us that Dr. Kerr is a thorough master of his subject, and a most inspiring teacher. His style is clear, forcible, and always interesting, and his methods of deduction are often novel and suggestive. Especial mention may be made of the sections on the acute infectious exanthemata, in which will be found, besides the careful working out of their diagnostic features, a statement of the principal complications to be looked for, and a study of their premonitory symptoms, the early recognition of which may mean so much in the final outcome of the case.

Dr. Kerr's work has been so well done that it seems ungracious to single out for criticism any expression of personal opinion or inadvertent statement; but the reviewer feels satisfied that in future editions, which are sure to come, some modification should be made in the statement that tuberculous meningitis is the commonest form of meningitis in childhood (p. 313). Clinical observation, aided by systematic study of the cerebrospinal fluid, certainly points to the greater prevalence of meningococcic infection, even in those cases of slower onset which suggest the picture of tuberculous meningitis that has become classic. But this is merely a friendly hint, without malice. Dr. Kerr has done an excellent piece of work, and we feel certain that the student and the practitioner as well, can learn more of pediatrics from its perusal than from the ordinary text-book.

T. S. W.

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**THE CARE OF THE BABY. A Manual for Mothers and Nurses.**  
By J. P. CROZER GRIFFITH, M.D., Clinical Professor of Diseases of Children in the University of Pennsylvania, Philadelphia.  
Fourth edition; pp. 425; illustrated. Philadelphia and London: W. B. Saunders Co., 1907.

THE appearance of a fourth edition of Dr. Griffith's well-known manual emphasizes the favor with which it was originally received, and a careful comparison of texts shows that little was found in the third edition that could be improved upon in the fourth, except in the illustrations, which have been increased by ten. An appendix of sixteen pages, however, has been added, covering briefly the general principles of feeding a healthy infant, intended for mothers who, of necessity, are thrown entirely upon their own resources when this important problem confronts them.

This book should long maintain its distinction as one of the best of its class.

T. S. W.

# PROGRESS OF MEDICAL SCIENCE.

## MEDICINE.

UNDER THE CHARGE OF

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**The Blood in Myxœdema.**—BENEE and ENGEL (*Wien. klin. Woch.*, 1908, xxi, 905) report the blood findings in 5 cases of myxœdema. Frequently a mild secondary anemia is present. The most marked alteration occurred in the leukocytic formula. Differential counts showed the following: polymorphonuclear neutrophiles 58 to 39 per cent.; lymphocytes 36 to 56 per cent.; eosinophiles 4.9 to 15.8 per cent.; mononuclears 2.4 to 8 per cent. The eosinophilic myelocytes were found. Thyroidectomized animals show a lymphoid metaplasia of the bone marrow and this, Benee and Engel say, explains the lymphocytosis. The eosinophilia they look upon as the result of positive chemotaxis from substances circulating in the blood. The total number of the leukocytes was normal (one case 12,400).

**The Finding of Products of the Adrenals in the Blood and the Urine.**—WATERMAN and BODDAERT (*Deut. med. Woch.*, 1908, xxxiv, 1102) doubt the accuracy of previously reported observations, in which adrenalin in increased amounts is said to have been found in the blood and urine of nephritics, leading to the assumption of a hypersecretion of the adrenals in this disease. They show that the ferric chloride test for adrenalin may be given by pyrocatechin and salicylic acid, bodies closely related to adrenalin which is methylamido-acetopyrocatechin. The colors vary a little with these substances, that with salicylic acid being more violet, but in the pigmented urine or serum the color tests are unreliable.

Using Ehrmann's test (dilatation of the enucleated frogs eye) they find that pyrocatechin is strongly mydriatic (1 to 500 in 0.9 per cent. NaCl solution). Resorcin, hydrochinon, and salicylic acid are less powerful mydriatics. They have had no experience with Meyer's

test (the bloodvessel of a freshly killed ox is placed in the solution to be tested; if it contracts, adrenalin is assumed to be present), but Schlayer reported negative results with this test, using the blood and urine of nephritics.

Waterman and Boddaert conclude that the presence of abnormal amounts of adrenalin in the blood and urine of nephritics is, as yet, not satisfactorily demonstrated.

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**"Duodenal" Diabetes.**—EICHLER and SILBERGLEIT (*Berl. klin. Woch.*, 1908, xiv, 1172) based their study on a report by Zock, of two cases of glycosuria following the taking of alkali with suicidal intent. He observed that the duodenal mucosa was destroyed, while the pancreas remained uninjured. The production of a similar lesion is a dog also led to glycosuria, hence the assumption of a duodenal glycosuria in man and dog, the result of destruction of the duodenal mucosa.

Eichler and Silbergleit repeated Zock's experiment, using a somewhat different technique. After opening the abdomen aseptically, they injected 4 to 6 c.c. of concentrated sodium hydrate into the duodenum. Glycosuria resulted in 2 cases. In 2 other dogs glycosuria was produced by applying the Pacquelin cautery to the duodenal mucous membrane and destroying it. Other parts of the small intestine were next tried to see whether the action from destruction of the duodenal mucosa was specific. In 3 of 4 instances glycosuria ensued after lesions produced in the ileal mucosa. In all the dogs the pancreas showed nothing abnormal. The glycosuria was of short duration, disappearing on the fourth day after operation.

The authors look upon the glycosuria as being the result of the severe shock to the nervous system; the glycogen of the liver is thrown into the blood and is excreted in the urine. They conclude that it is not justifiable to speak of "duodenal diabetes" in man or dog.

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**Chyluria.**—LÜDKE (*Münch. med. Woch.*, 1908, lv, 1369) reviews the cases of non-parasitic chyluria reported in the literature and reports one new case, which followed a colon bacillus cystitis. No etiological factor could be found. There was no chylemia; diet had no effect in increasing or diminishing the fat content of the urine. The daily excretion of fat in the urine amounted to 6 to 8 grams. The prognosis is not unfavorable. No effective remedies are known. The condition is very rare.

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**A New Function of the Pancreas and its Relation to Diabetes Mellitus.**—LOEWI (*Arch. f. exp. Path. u. Pharmacol.*, 1908, lix, 83) has studied the mydriatic action of adrenalin in animals after the extirpation and after partial destruction of the pancreas in cats and dogs. In these animals normally one finds no mydriasis after instillation of adrenalin solutions. When the pancreas has been extirpated, he finds that adrenalin solution now has a mydriatic effect. Partial destruction of the pancreas gave inconstant results, mydriasis being present in some instances—absent in others. Loewi now instilled adrenalin into the conjunctiva of man. Three drops of 1 to 1000 adrenalin solution was used and the dose was repeated in five minutes. The pupil was carefully measured; the results showed, however, that when mydriasis

occurred it was visible to the unaided eye. In 36 cases—healthy adults, as well as those suffering with nephritis, carcinoma, tuberculosis, anemia, icterus, heart disease, adiposity, pneumonia, tabes, and rheumatism—no mydriasis was observed. Of 3 cases of Basedow's disease, 1 showed a marked dilatation of the pupil, due, the author believes, to increased irritability of the sympathetic. 18 diabetics were now examined. In 8 cases the instillation was without result; these included mild and severe diabetes: 1 patient in coma who had previously given a positive response, and 1 case of diabetes with acromegaly. In the 10 remaining cases of diabetes mellitus a marked dilatation of the pupil occurred within thirty to sixty minutes after instillation of the adrenalin, the cases ranging from mild to severe, including 1 in coma. Loewi concludes that (1) a positive test means pancreatic disease; (2) in a diabetic it indicates pancreatic diabetes; (3) the absence of the reaction does not exclude the pancreatic origin of the disease.

#### **The Importance of Urobilinuria in the Diagnosis of Diseases of the Liver.**

—FISCHLER (*Munch. med. Woch.*, 1908, lv, 1421) has studied the cases of urobilinuria and urobilinogenuria in Krehl's clinic, with interesting results. Urobilin and urobilinogen are formed from bilirubin in the intestines by the reducing action of bacteria. Both are absorbed and carried again into the liver. Fr. Müller's observations are the basis of subsequent work; in a patient with complete closure of the ductus choledochus, he showed that there was abundant bilirubin, but no urobilin. The patient was then given bile by the stomach tube, and in three days urobilin was found in the urine in addition to bilirubin. The same results have been obtained experimentally in dogs. Normally, urobilin and urobilinogen are absent from the urine or are present only in traces. They are found in the urine practically only in those conditions in which the liver is diseased, according to Fischler's observations. The tests for these bodies are of importance in the diagnosis and prognosis of obstructive jaundice, since they enable one to determine whether any bile enters the intestine. In Laennec's cirrhosis of the liver these bodies are always present in the urine, and their presence or absence may be important differential diagnostic signs of this disease. So, too, in chronic passive congestion of the liver, acute infectious diseases, pulmonary tuberculosis, the presence of urobilin indicates that the liver is diseased.

**The Spectroscopic Determination of Blood in the Urine.**—SCHUMM (*Munch. med. Woch.*, 1908, lv, 1488) calls attention to several points which may prove helpful in detecting minute quantities of blood in the urine. In making spectroscopic examination of the urine for blood, he points out that it may be recognized in quantities as small as 1 to 2000, when the urine is contained in the usual test tube; if the layer of urine through which the light must pass is made much thicker, the delicacy of the test is greatly increased. Thus when urine is put into the usual polariscope tube of 20 cm. length, the bands of oxyhemoglobin may be recognized in a dilution of 1 to 25,000 (amounting to about one drop of blood in the twenty-four-hour urine). If oxyhemoglobin has been changed to methemoglobin or hematin, the urine must first be extracted and then examined for the bands of hemochromogen.

**The Stomach Contents in Gastric Carcinoma.**—H. FISCHER (*Deut. Archiv f. klin. Med.*, 1908, lxxxiii, 98) studied protein digestion produced by the gastric juice, obtained from 2 cases of carcinoma of the stomach, each a year old. Normally, the gastric juice does not split protein to di-amino-acids, and it is as yet unsatisfactorily shown that monamino-acids are formed. In gastric carcinoma, on the other hand, Fischer has demonstrated that a ferment is present capable of splitting the proteins into mono- and di-amino-acids. This, then, may prove of value in the diagnosis of gastric carcinoma, after a simpler technique for the recognition of di-amino-acids is found. The puzzling HCl deficit in gastric carcinoma is also explained by Fischer's experiments. Emerson's experiments seemed to show that alkaline bodies arise in gastric cancer, but at that time Emil Fischer had not demonstrated that the protein molecule is formed of amino-acids linked together (smaller groups, peptides). In carcinoma the HCl unites with the amino radicle, the body thus formed reacting acid to litmus, whereas, the peptid ununited with HCl is alkaline to litmus. The result in gastric carcinoma is that the total acidity increases, free HCl disappears; indeed a point is reached where the HCl present no longer suffices to satisfy all the free amino groups, that is, where HCl must be added to neutralize the amino-radicles before the reaction for free HCl is obtained.

**The Use and Value of Tuberculin in the Diagnosis of Pulmonary Tuberculosis.**—L. HAMMAN (*Archiv. of Inter. Med.*, 1908, i, 443), after a complete review of the previous literature of this subject, gives in detail the results in many cases of the subcutaneous, eye, and skin tuberculous reactions and concludes that while tuberculin is a valuable aid in the diagnosis of pulmonary tuberculosis, it must be used with care and the results interpreted with caution. The reaction is specific, and it must be borne in mind that a very insignificant lesion may produce tuberculin hypersensitiveness; the prevalence of such lesions should be fully realized. A negative reaction is decisive information as is also a focal reaction. In the absence of a focal reaction, tuberculin hypersensitiveness must be valuable as one phase of the clinical picture, and our judgment not too much warped by its presence. The cutaneous reaction is too delicate an indicator to be of any value in diagnosis unless the reaction be negative, which it seldom is in adults. The eye reaction gives results more nearly in accord with clinical experience, but by no means absolutely certain, and Hamman feels that it cannot supplant the subcutaneous method. In comparing the last two methods, they should not be used simultaneously; the eye inoculation should precede the subcutaneous by at least a few days.

**The Gastric Secretion in Nephritis.**—ENRIQUEZ and AMBARD (*Sem. méd.*, 1907, xxxv, 409) note that deprivation of salt in diets has an effect on the gastric secretions both in cases of hyperchlorhydria and hypochlorhydria, causing, in both instances, a drop or increase in the hydrochloric acid and so a return to the normal secretion or thereabouts. Enriquez and Ambard claim that every nephritis has a more or less marked influence on the gastric secretion. In very slight kidney lesions there is usually manifested a hyperchlorhydria, this being most probably due to the excess of salt in the body which salt stimulates the

gastric secretion. Retention of salt then increases the secretion and deprivation of salt reduces it, as has been shown experimentally in dogs. In more severe nephritis with albuminuria, however, the retention of salt alters the gastric secretion, but this excess of salt has an irritating effect on the stomach as on the kidneys; this irritating and therefore depressing action overcomes the stimulative action which would produce a hyperchlorhydria and so hypochlorhydria results. The deprivation of salt then allows the stomach mucosa to recover its tone and overcome this depressant action even before the general salt balance throughout the body is restored. Thus dechloridation may be followed by a slight, transient hyperchlorhydria. Enriquez and Ambard believe that the effect of salt deprivation on altered secretions of the stomach opens up a new field for the study of its many diseases, and may have great influence on some of the modes of treatment in gastric disorders which at present have no apparent connection with each other.

**Excretion of Urotropin in the Bile and Pancreatic Juice.**—S. J. CROWE (*Johns Hopkins Hosp. Bull.*, 1908, xix, 109) notes that for many years substances excreted in the bile have been more or less carefully studied in the hope of finding a suitable antiseptic capable of being excreted in sufficient strength to act favorably in injections. The part played by the typhoid bacillus in the gall-bladder, whether as an infective agent, as in the dangerous chronic carriers of disease, or as the starting point of gallstones, led Crowe to experiment with urotropin (hexamethylenamen), which has been already used so successfully in bacilluria and can so easily be detected by tests. In the animals experimented upon it was found that urotropin, when administered by mouth, was rapidly absorbed and remained in the circulating blood twenty-four hours, with a maximum concentration five to eight hours after giving the drug. In dogs it is excreted in the bile, pancreatic juice, and directly through the wall of the gall-bladder. It was found to be present in the saliva and milk of dogs after the intravenous injection of 1 gram. With this experimental data at hand Crowe was able to study the effects of this drug on several surgical cases with biliary fistulæ. These cases showed a rapid disappearance of the organisms from the infected bile following the use of the drug, and the fistulæ closed rapidly. In another case in which the injection was made into the cerebrospinal fluid, and in one case of gonococcal arthritis the infection rapidly cleared up on the administration of the drug. Crowe was able to demonstrate its excretion in the bile, cerebrospinal fluid, saliva, pleural exudate and the blood in man; he also found that after single large doses, 75 grains per diem, it appears in the bile in quantities which exercise a decided bactericidal action. The large doses in the cases studied caused no gastric symptoms or no hematuria, but in one case there developed painful and frequent micturition which stopped promptly on withholding the drug for a few days. Crowe believes that the drug may be of great value in acute affections of the gall-bladder, as a prophylactic in typhoid convalescence, against the possible subsequent formation of gallstones or the development of chronic bacillus carriers, and, lastly, as a general prophylactic before gall-bladder operations.

## SURGERY.

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UNDER THE CHARGE OF

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**Concerning the Experimentally Produced Ulcer of the Stomach.**—CLAIRMONT (*Arch. f. klin. Chir.*, 1908, lxxxvi, 1) says that up to the present time no one has succeeded in producing, experimentally, a gastric ulcer in animals. By the excision of a piece of mucous membrane, and cauterization with acids (Fibich), stomach defects result which never fail to heal and, therefore, do not develop into genuine gastric ulcers. In the cardiac half of the stomach the healing occurs more rapidly, as a rule, in three weeks the defects are covered with epithelium, than in the region of the pylorus where the cicatrization is concluded usually in six or seven weeks. Either by a simultaneous or a later performed gastro-enterostomy, the process of regeneration is favorably influenced and leads to a more rapid healing of the defect regardless of what portion of the stomach it may involve. Fibich's view, that a gastric ulcer after a gastro-enterostomy heals like a fresh defect in the mucous membrane in a few days, is not supported. The postoperative treatment, after a gastro-enterostomy, must take into consideration that the ulcer still remains and that it must gradually become cicatrized.

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**Concerning the Origin of Lateral Cervical Fistulæ.**—WEGLOWSKI (*Zentralbl. f. Chir.*, 1908, xxxv, 426) says that the lateral cervical fistulæ are very similar in formation to the median fistulæ. In both there may be several lumina and in both the lining is usually of cylindrical epithelium, although several layers may be found. Lymphoid follicles, mucous glands, etc., are found in their walls. While the median fistulæ are recognized as developing from the thyroglossal duct, the lateral are considered as originating from the branchial clefts. This latter theory does not explain why the external openings are found only along the anterior border of the sternomastoid muscle, and why it is found at times at the angle of the lower jaw, at times at the sternum. Nor does it explain, why, with an opening for example in the middle of the neck, its course is not always upward, but often downward toward the sternum. Weglowski made a series of investigations on embryos, as well as on cadavers, and found a complete analogy between both kinds of fistulæ. The branchial clefts disappear in the second month of embryonal life. From the first arch is formed the lower jaw, and from the remaining three arches are developed the body, horns of the hyoid bone, the styloid and similar muscles. The branchial apparatus is properly limited to



the region of the face, not to the neck. The hyoid bone determines the lower border of the branchial region. Neither the arches nor clefts can project themselves downward, and, therefore, remnants of them cannot be found in the neck. The abnormal situations of the external cleft with relation to the inner, which usually have been made to explain the etiology of these fistulæ, have not been observed in embryonal life. In the third week of embryonal life there appear two depressions which become canals leading downward. One springs from the third cleft, the other from the fourth. From the third is developed the lateral lobe of the thymus gland, and from the fourth the thyroid. Weglowski's investigations on the cadaver showed that in 14 per cent. some remains of the canals of the thymus gland were found from the throat to the sternum. Remains of the thyroid were found in only 2 out of 150 preparations. The conclusion is reached that the lateral cervical fistulæ arise not from the branchial clefts, but from the remains of the of the thymus and thyroid glands.

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**The Operative Treatment of Varicose Veins, Elephantiasis, and Ulcer of the Leg.**—FRIEDEL (*Arch. f. klin. Chir.*, 1908, lxxxvi, 143) treats those cases of varicose veins of the lower extremity, which are not suitable for excision or the Trendelenburg operation, by a spiral incision. The varicose veins tend to increase in size and extent and may become imbedded in cicatricial tissue from repeated inflammation, and may become concealed in an extensive concomitant œdema producing an elephantiasis of the leg. Often the patient is weakened and run down. Previous ligature may have failed and the associated ulcers may refuse to heal under the usual hospital treatment. In such cases Friedel has obtained good results from the spiral incision of Rindfleisch. The operation is performed in suitable cases as follows: Anesthesia is produced by lumbar spinal injection. Then in all cases a piece of the saphenous vein is excised, and the course of the spiral incision is marked by a light scratch of the skin of the leg. If an ulcer has been or is present, its site is included between the spirals of the incision, above and below, the chief point is to divide all the varices, and, if possible, several times. The incision should begin high enough, usually just below the knee, and should go as low as necessary, usually to the dorsum of the foot. The closer the turns of the spiral incision are to each other, the more often the individual veins will be divided and the greater the possibility that the varices will be entirely removed. While Friedel was satisfied with two turns at first, he later employed five. Bad results, as skin necrosis, have not resulted from the close approximation of the spirals, and in the future he will probably place them closer together. In this way he hopes to remove almost entirely the pressure within the vessels. The extensive opening up of the lymph and connective-tissue spaces causes an enormous evacuation of the serum of the field of operation. This leads to a subsidence of the inflammatory symptoms, and a reduction of the swelling of the limb. The frequency with which the blood stream is broken gives greater security against recurrences.

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**An Operative Treatment for Obesity.**—SCHULZ (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1908, xviii, 776) says that he has found no published record of operation for obesity since Demars and Marx in 1890. He

reports good results in 2 cases operated on five and four and one-half years ago. The layer of fat in the abdominal wall is not equally thick in all parts. In the lower part, above the pubic and inguinal regions, it does not exceed in thickness more than about one inch. Elsewhere it varies widely. Where these two regions, one of constant the other of varying thickness of fat, meet, are two curved lines each passing from one anterior superior iliac spine downward and inward toward the pubis. The overhanging fat produces furrows at the lines, and is further forced downward in women by the use of corsets. The furrows mark the position of the lower transverse incision, the upper in the median line being two fingers' breadth below the umbilicus and passing to both sides well to the lateral portion of the back. The lower meets the upper at its ends. The intervening elliptical portion is removed down to the aponeurosis. The point in the median line, through which the upper transverse incision is to be made, is determined before the operation, while the patient is standing and the overhanging roll of fat can be best observed. When the patient is lying down this cannot be well determined. After the removal of the skin and fatty layer, included between the incisions, it will be seen that the thickness of the layer of fat in the upper cut surface is much greater than that in the lower. A wedge-shaped piece of the fat is removed from the upper wound surface, the incision for this being directed from the skin obliquely to the aponeurosis. The skin edge of the upper flap can then be drawn more easily toward that of the lower and the wound closed by sutures. Two drains are passed from the median line to the ends of the wound. A large amount of fatty material will escape through the drains. If this were retained it would favor suppuration. The operation is so easily carried out, there is so little danger associated with it, and the results are so good that in the future it should gain more general favor.

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**Treatment of Perforative Peritonitis.**—MURPHY (*Annals of Surgery*, 1908, lxvii, 870) says that the importance of the peritoneum lies not so much in its great surface as in its tremendous power of absorption. There is early acceleration of absorption with slowing later on. I we can tide our patients over this period of accelerated absorption all will be well. The term "free" peritonitis should be used for the general, diffuse variety, and "circumscribed" for the encapsulated form regardless of the size. Of the typical symptoms, collapse is a later, never an initial, symptom. The patient should be placed in the Fowler position as soon as the diagnosis is made and kept so until convalescence is well advanced. The relief of pus tension is the first surgical step toward retarding absorption in all acute infections. Reduction of tension should be initial and the absence of pressure continuous. These are accomplished by drainage. The entire technique of these operations for peritonitis must be accomplished in a very few minutes, that is, get in quick and get out quicker. The retention of fluid (proctoclysis) depends entirely on the method of administration. Opium and coal-tar products were never given in this series of 51 cases. Of these there were 6 of postoperative ileus; 2 were operated on for gastric perforations, 1 duodenal, 5 typhoid, and 43 appendiceal. One died of a double pneumonia on the sixth day after operation, and a second from mechanical ileus. The time elapsing between the perforation and the operation

varied considerably. In the duodenal case it was eight hours; in the gastric cases it was eight and fourteen hours respectively. In the appendiceal cases a period of forty hours was not exceeded, while many of them had suffered from the appendicitis, three, four, up to seven days. There was no death in the series of 51 cases from the peritonitis; *per se*.

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**Late Results after Operation for Benign Diseases of the Stomach and Duodenum.**—MOYNIHAN (*Annals of Surgery*, 1908, xlvii, 873) made an analytical study of 281 cases upon which he had operated for non-malignant diseases of the stomach, up to the end of 1905. The following are some of the lessons to be learned from this study: The operative treatment of stomach disorders should be confined exclusively to those cases in which an organic lesion is present, such as a demonstrable and palpable ulcer of the stomach or duodenum or some condition which hampers the proper action of the stomach. When at operation a perfectly normal stomach is found, we must not cover our diagnostic failure by the performance of an unnecessary operation. In cases of acute perforating ulcer the perforation should be closed or the ulcer excised. When the ulcer is on the lesser curvature nothing more is necessary. When it is prepyloric, pyloric or duodenal, gastro-enterostomy also should be performed. When a non-malignant lesion is discovered the appropriate treatment depends upon its position in the stomach. An ulcer on the lesser curvature, some distance from the pylorus, offers no obstruction to the passage of food and should be excised. A gastro-enterostomy may give incomplete relief, and malignant disease may set in later. In some cases, however, when the ulcer is on the curvature or on the posterior surface of it, adherent to the pancreas, relief follows if gastro-enterostomy is performed on the cardiac side of the lesion. Gastro-enterostomy should be performed if the ulcer be perpyloric, pyloric, or duodenal. It should be infolded whenever possible to prevent hemorrhage and perforation. The most satisfactory method of gastro-enterostomy is the no-loop operation, with the almost vertical application of the bowel to the stomach. Regurgitant vomiting occurs as the result of the "loop" operation, whether anterior or posterior. It is relieved almost certainly by an entero-anastomosis. In cases of hour-glass stomach, the surgical treatment necessarily presents special difficulties on account of the frequency of two lesions: one in the body of the stomach and one at the pylorus, and double operations have to be frequently performed.

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**A New Method of Diagnosis and Treatment of Fistulous Tracts.**—BECK (*Zentralbl. f. Chir.*, 1908, xxv, 555) injects a bismuth-vaseline, a paste of a fluid consistency, under aseptic precautions, by means of a glass syringe, into the fistulous tract under considerable pressure. By the skiagraph he is then able to trace the fistula to its origin, usually to diseased bone. Operation is then always successful. In one case the injection was followed in a short time by healing of the fistula, although it had existed for two years and was due to tuberculous disease of the second and third lumbar vertebrae. The fistula has remained closed for two years. A similar result was obtained from a fistula in an old coxalgia, for which several radical operations had been done

during a period of four years. This result was repeated in a third case, a tuberculous osteomyelitis of the knee. During two years' experience with this method many other cases were treated successfully. Of special interest was a case of empyema of the pleural cavity, which discharged four ounces of pus daily for nine months. It failed to improve under any treatment, and, finally, an Estlander operation was proposed. After ten injections given every other day, the fistula was completely healed and remained closed for three months, showing no signs of retention. Beck explains the results upon the principle of affording a scaffolding for the granulations and the subsequent cicatrix formation. He expects later to study the exact pathological findings and to report the results. Two bismuth mixtures are employed: one for diagnostic purposes and the other for later treatment. That for diagnosis consists of bismuth subnitrate 30 parts, and white vaseline 60 parts. That for the later treatment is made up of bismuth subnitrate 30 parts, white vaseline 60 parts, paraffin, soft, 5 parts, and wax 5 parts.

**Two Cases of Traumatic Urinary Effusions in the Renal Region (Traumatic Pseudohydronephrosis).**—NOVE-JOSSERAND and BALLIVET (*Arch. gén. d. chir.*, 1908, ii, 437) report two cases, in children resulting from a fall, of this relatively rare condition. In both an incision was made through the abdominal wall over the tumor, opening the peritoneum, through which the tumor was recognized as occupying the renal fossa. It was opened and evacuated and the margins of the opening in the tumor sutured to the edges of the parietal peritoneum of the abdominal incision, with drainage. The first patient recovered and the second died. An autopsy on the latter showed a stricture of the ureter about 15 cm. from its termination in the bladder. Of Monod's 27 cases, in 22 the age was noted and in these it occurred 13 times in children under fifteen years of age. It was the result of varied traumatism. In almost all cases there was immediate pain more or less acute, accompanied by a mild grade of shock, without grave peritoneal disturbances or any of the classical signs of hemorrhage. In 2 of Monod's cases and 1 of the authors' the painful phenomena were completely absent. In 12 out of 27 cases the pain was accompanied by hematuria, always slight and coming on immediately or two or three days after the accident. The appearance of the tumor is never immediate, in the earliest case developing in ten days, ordinarily in only twenty to thirty days after the accident, sometimes after fifty to sixty days. It may progressively increase until it fills the loin space and passes over the median line anteriorly. It is largely filled with urine. The authors recognize two groups of cases: the first consisting of simple cases without preliminary lesions of the urinary apparatus, and the second of complex cases with persistent lesions of the kidney, ureter, or pelvis. When in the simple there is a small perirenal effusion without disturbing functional symptoms, one may wait, as a spontaneous cure may follow. If it persists one, two, or three successive punctures may be made. In case of incessant reproduction of the effusion, incision and marsupialization should be resorted to as in one of the authors' cases. Only exceptionally will nephrectomy be necessary. In the complex cases spontaneous cure has not been observed. A free opening should be made.

## THERAPEUTICS.

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UNDER THE CHARGE OF

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**Serum in Scarlet Fever.**—CUMSTON (*British Medical Journal*, 1908, i, 1291) concludes his observations of the serum treatment of 42 scarlet fever patients with the statements that the recovery rate seemed better than usual, and that the earlier the serum was administered the better were the results. In many instances within forty-eight hours of the injection the temperature began to fall, the cervical glands began to subside, the necrosis of the throat began to clear, and the rhinorrhœa ceased or lost its purulent character. Not all patients did so well as this, but most did very much better than would have been expected under ordinary treatment. The author has the distinct impression that the injection of antiscarlatinal serum in doses of not less than about 12 drams, and as soon as the onset of nasal discharge, glandular swelling, fever, and signs of sepsis occur, will produce a marked improvement in septic instances of the disease. In the toxic type little can be said in favor of the use of the serum.

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**Psychotherapeutics.**—DERCUM (*Therapeutic Gazette*, 1908, xxxii, 305) states that in applying psychotherapeutic methods we should always remember that the patient's symptoms have a physical basis: this is especially true in functional nervous diseases. States of exhaustion play a fundamental role in all of them, and when the general level of the mental tone is raised obsessions disappear. It would seem, then, that attention to the physical condition of the patient, the bringing of his health to the highest level, must be the first object of our treatment; in other words, simple physiological procedures, rest, full feeding, gentle exercise, bathing, massage and the like, should always be instituted. In obsessional states there is essentially a neurasthenia, or, to use the latter-day term, a psychasthenia; it is the underlying asthenia which first demands our attention. Rest and physiological measures can be applied in accordance with the character of the patient, from partial methods up to a full rest cure. Added to these conditions we should institute such simple psychotherapeutic measures as mental rest, especially such as is secured by the isolation of the patient; second, the restraining of the patient; later special mental exercises or mental gymnastics, if necessary. During all of the time judicious use should be made of normal suggestion, both direct and indirect. Under the latter we should include such an explanation to the patient

of his condition as may be adequate and tactful, pointing out that his symptoms are functional, and that they will in time disappear. That normal suggestion acts powerfully when the general health is improving goes without saying. Suggestion under hypnotism is rarely if ever justified. Psycho-analysis will probably, for reasons already given, never find a permanent place in our therapeutics.

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**The Alkalies in Bronchial Catarrh.**—HAIG (*British Medical Journal*, 1908, i, 1100) has been accustomed to employ the salicylates in bronchial inflammations attributed to uric acid irritation or rheumatism. He finds that this form of treatment fails when the urinary acidity is low, and as the effect of dyspnoea, from which these patients often suffer, is to increase the alkalinity of the blood and lower the acidity of the urine, it follows that the salicylates will fail when dyspnoea is considerable and cardiac dilatation is beginning. Noting this, Haig began to try the alkalies in such patients, and found that it was only necessary to give the alkali in sufficient dosage to render the urine alkaline to bring about immediate relief in many instances. The alkali preferred is sodium bicarbonate in twenty-four hour dosage of 20 to 60 grains for a child and 90 to 120 grains for an adult. The alkali should not be combined with drugs which raise the urinary acidity or which act as a precipitant of uric acid, such as lime, the metals, or their salts, or even the chlorides, sulphates, or nitrates of the alkalies. Ammonium particularly should not be given, for it raises the urinary acidity and its urate is insoluble.

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**Rectal Injection of Antitoxic Sera.**—PARKINSON (*Lancet*, 1908, i, 1273) advises the rectal administration of sera in those patients who object to the prick of the needle, and because when sera are given in this way there are never any untoward accidents such as may occur after hypodermic injections. He states that it is not certain that the rectal lining is absorbent of therapeutic sera, but asserts that their effects are quite as evident when given per rectum as when given in the more usual way. His technique is as follows: Cleansing enemas are not given unless there is marked constipation. The patient lies on the left side and a catheter is passed as far as possible into the rectum. To the catheter is attached a glass urethral syringe containing the serum. The fluid usually will flow in of itself, but if necessary the piston is used. After the injection the patient should remain in the recumbent for fifteen minutes. Instances of the administration of anti-streptococcic serum and of diphtheria antitoxin are cited.

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**Psychotherapy in Functional Neuroses.**—HERRING (*New York Med. Jour.*, 1908, lxxxvii, 885) discusses this subject, in part, as follows: After a thorough physical and mental examination of a patient the physician assures himself that the affection is entirely functional; he can then institute rational psychotherapy and use as adjuncts the necessary physiological means to bring about a cure. Using either persuasion or suggestion, or both, because it will be a difficult matter to separate the two, he will state plainly the facts of the case to the patient, telling him what caused the trouble and explaining how the symptoms may be produced, the part the mind plays in originating and

fostering the various fears and distressing symptoms. The fact that these can be relieved and cured with his coöperation, and how this is to be brought about, are impressed upon him repeatedly. Patients of average intelligence will listen to this with interest, and the majority will enter into hearty coöperation with the doctor. The average patient will accept the statement of the physician, and will believe that he will get well, even after months of suffering. After once carefully listening to a recital of the symptoms and explaining each one, it is much better at subsequent visits not to refer to them again or allow the patient to refer to them. Keep the one idea always in view that the symptoms will disappear and that entire recovery will take place. When the patient requires treatment other than that which is purely psychic, one should not hesitate to use dietetics, electrotherapy, hydrotherapy, pharmacotherapy, or any physiological means to bring about recovery. Psychotherapy should not tend to make us therapeutic nihilists.

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**Serum Treatment of Exophthalmic Goitre.**—BLUMENTHAL (*Folia Therapeutica*, 1908, ii, 62) has used both an antithyroid serum, which represents the blood serum of thyroidectomized sheep, and an alcohol-ether precipitate of the milk of thyroidectomized goats in the treatment of this disease, and finds that the former is decidedly more potent than the latter. The dose of the serum is, at first, 10 drops thrice daily, increased to double this amount, gradually dropped to 5 drops, three times a day as improvement takes place. Sometimes the serum causes palpitation, in which case the less active powdered precipitate is substituted; its beginning dosage is 75 grains per day increased gradually to six times this quantity. The dosage must be varied in accordance with the patient's response to the treatment. The serum is usually well borne and its administration usually results in a softening and sometimes in a diminution in size of the thyroid gland; the oesophageal and tracheal pressure for the most part ceases, and the exophthalmos becomes less marked, although the tachycardia often remains uninfluenced. The treatment always influences the subjective symptoms, the insomnia yields, in most instances, within a few days, the perspiration diminishes, the palpitation and feeling of distress improve and the body weight is increased. It is of course necessary to continue the treatment for months or years. The great disadvantage is that the improvement may be so slow that the patient becomes discontented and unwilling to persist in it. The author considers that this treatment is preferable to operation on account of the danger of the latter and since the end-results of surgical interference are not completely favorable.

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**Organotherapy in Exophthalmic Goitre.**—RENON and DELILLE (*Tribune Méd.*, 1908, xli, 281) have employed the extract of the hypophysis in this disease on account of the known effect of this substance upon arterial tension, tachycardia, and the thyroid gland. A number of their patients have been benefited, but no cures were effected. It appears logical to treat exophthalmic goitre with the glycerinized blood of animals deprived of the thyroid gland combined with pituitary extract, since hemato-ethyroidine neutralizes the effect of thyroid hypersecretion and since the pituitary body exercises a general vasoconstrictor effect. The two treatments may be associated by giving the patient each day

2 to 3 teaspoonsful of hemato-ethyroidine and 3 to 6 grains of powdered pituitary extract. After twenty days of treatment an interval of eight days is advised; other series of treatment are prescribed in accordance with the effect produced. Another method is to administer the hemato-ethyroidine alone for fifteen days, after which the pituitary extract is given for a similar period. This combined organotherapy based on physiological, pathological, and general therapeutic principles gives better results than either form of treatment alone, and causes remarkable remissions in the symptoms of exophthalmic goitre.

**The X-rays in Leukemia.**—TAUSSIG (*Interstate Med. Jour.*, 1908, xv, 439) reports three instances of leukemia treated by the Röntgen-rays and sums up our knowledge of this form of treatment as follows: Reports of apparent cures of leukemia by means of the x-rays were received with great enthusiasm, and it was believed that a cure for this disease had been discovered, but, unfortunately, these sanguine expectations have not proved well founded. One after another, the patients, thought to have been cured, relapsed and died, so that it seems established that in the x-ray treatment of leukemia we have a palliative, never a really curative, agent. Nevertheless it is our most potent therapeutic method in this disease. It would seem that in myelogenous leukemia the rays exert a favorable influence in about 90 per cent. of patients. The patients become subjectively well and only the demonstration of a slight splenic tumor and of an occasional myelocyte in the blood serve to remind us that the disease is only latent. Sooner or later the inevitable relapse occurs and then the rays usually prove far less effective than at first; the total duration of the disease is still usually less than one year, rarely more than two, but meanwhile the patient has had months of apparent health. In lymphatic leukemia the rays have proved far less effective than in the myelogenous type. Here the blood is but slightly affected and only those lymph nodes which have been directly exposed to the rays show any tendency to atrophy. Occasionally, however, results have been obtained rivalling those in myelogenous leukemia. At all events, even in lymphatic leukemia, the x-ray treatment deserves a trial.

**Marmorek's Serum in Tuberculosis.**—UHRY (*Revue Francaise de Méd. et de Chir.*, 1908, vi, 135) has treated 48 patients with Marmorek's serum; of these 11 were affected with surgical tuberculosis and 37 were the subjects of pulmonary tuberculosis in different stages. Of the 11 instances of surgical tuberculosis, 10 were cured and 1 was greatly benefited. Of the 15 instances of pulmonary tuberculosis of the first degree 13 were cured; notable amelioration took place in 2 who have been so lately treated that further prognosis is uncertain. Of 21 patients in the second and third stages 3 were entirely cured, 10 much improved, and 8 have died. No untoward effects of any consequence were observed during the treatment even when daily doses as large as 6½ drams were employed. Slight pain at the site of the injections sometimes was noticed and twice a slight urticaria was remarked. The treatment seems to be absolutely harmless.



## PEDIATRICS

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UNDER THE CHARGE OF

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**Whooping-cough, Complicated by Acute Nephritis, Lobular Pneumonia, and Left-sided Hemiplegia.**—This remarkable case, which terminated in recovery, is reported by A. E. BLACKBURN (*Jour. Amer. Med. Assoc.*, 1908, i, 530). A child, aged four and one-half years, had been suffering with whooping-cough for six weeks, during which time he was not under the care of a physician. He spent a great deal of time in the open air during a period of extreme dampness and cold. He was seized suddenly with a general convulsion, followed immediately by coma. Other causes having been eliminated, the child was catheterized and albumin in large quantities found in the urine. During the uremic state the temperature rose to 108°, the child was pulseless, and respirations were very high. The coma lasted for ten days. A few days later the right upper lobe showed signs of consolidation anteriorly, and during this the temperature again rose to 107°, the pulse again became impalpable and death seemed imminent. Inability to expectorate several times almost caused death through strangulation, but the crisis was safely passed, when constant convulsive movements were noticed in the right side; the right arm and leg could be moved, but not the left. A complete left-sided paralysis, involving the left arm, leg, side of the face, and the left external rectus was noted as the child became sufficiently conscious. The nephritis gradually disappeared, the pneumonia resolved, and the cough again became whooping in character; it finally disappeared. Seven months after the onset the patient walked with a halt and the left arm was weaker than the right; otherwise he had completely recovered. The stimulation throughout was rather vigorous for a child so young.

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**A New Constituent of Milk (Lactoconium).**—A. KREIDL and A. NEUMANN (*Wien. klin. Woch.*, 1908, xxi, 214) report examining the milk of different species (cow, rabbit, guinea-pig, dog, cat, and woman) with the ultramicroscope. They discovered in the milk of the lower animals a corpuscular constituent, which they could not find in the milk of woman. The milk of the animals contained a large number of small particles, which were in constant violent molecular movement. These the authors propose to call lactoconia, until their true nature is discovered.

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**Parathyroid Meningitis in Infants.**—Two such cases are reported by L. ARTZ and J. BOESE (*Wien. klin. Woch.*, 1908, xxi, 217) in infants respectively seven weeks and five months old. In both cases the primary conditions had been gastro-enteritis, in the course of which the meningitis developed. In both instances Gram-positive cocci were isolated, which, in the second case, at least, could positively be identified with the paratyphoid bacillus of Schottmüller. It was agglutinated

by the immune serum from the *Bacterium paratyphus* Schottmüller B., and the serum from it agglutinated the corresponding emulsions of bacteria. The agglutination was noted in as high a dilution as 1 to 24,000, the exposure being one-half hour at room temperature. In the case of the coccus from the first case agglutination occurred only in dilutions of 1 to 1000, but in spite of this a similar conclusion could be arrived at. This shows that paratyphoid infections occur at a very early age, probably by way of the intestinal tract and lead to a bacteremia. As there are many cases of fibropurulent meningitis in childhood, the authors suggest, in view of the already large number of cases of typhoid and colon meningitis described in children, that all bacteriological and serodiagnostic aids should be employed to discover the exact nature of every case of meningitis in infants and children.

**The Influence of Thyroidal Feeding upon the Nitrogenous Metabolism of Children.**—A. ORGLER (*Zeit. f. exper. Path.*, 1908, v, 1) performed his experiments to determine the influence of large amounts of thyroid substance upon the general health, the pulse, and respirations of infants and children. The usual reports are that they react entirely differently from adults; another object of his observations was, whether they do not react at all or simply compensate the injuries better. The amount of nitrogen and uric acid was determined; four children were given large quantities of fresh thyroidal substance, two others were given potassium iodide, and one iodeigon; the latter to determine the influence of an organic iodide, and artificially iodized albumin. In addition to the thyroid gland, the children were given only milk and zwieback. The general health of all remained perfectly good in spite of the large amount of thyroid gland given; the pulse and respiration were not influenced in the slightest. In every case a larger amount of nitrogen was excreted, however, than was taken in. In the case of the three children given iodides and iodeigon, the nitrogen excretion was not increased. The body weight in two of the children fed with thyroid decreased; in the others it remained stationary.

**The Value of the Suprarenal Glands in the Pathology and Treatment of Rachitis.**—Stoelzner, after feeding a number of children at the Berlin pediatric clinic with suprarenal substance, reported marked improvement in rachitic symptoms due to retention of calcium salts. The symptoms which, in particular, improved were the sweats, craniotabes, slow dentition, sensitiveness to pain, restlessness, and vasomotor irritability; the children learned to sit, stand, and walk at a much earlier period than other rachitics. The abnormality of the thorax and vertebral column diminished, the fontanelle became smaller, the rachitic rosary and the epiphyseal swellings of the long bones disappeared. Stoelzner believed this improvement to be due to the retention of lime salts after feeding with suprarenal substance. To note the truth or falsity of this theory R. OUEST (*Zeit. f. exper. Path.*, 1908, v, 43) performed a number of experiments with young dogs, determining the excretion of the calcium and the nitrogen. He could not determine a retention, but could observe an unfavorable influence upon the calcium metabolism, which lasted not only while the dogs were being fed, but also for some time after. A number of clinical observations have also refuted the theory of Stoelzner, and it therefore seems probable that suprarenal

extract has no more influence on rickets than have other organic substances as thyroïdin, thymus extract, etc. The glycosuria and arteriosclerosis noted in these and other reported experiments are due not only to increase in blood pressure, but much more so to a toxic action of the adrenalin upon the entire organism.

**Rennet Coagulation in the Stomach of Nursing Infants.**—The question whether the cheese clots forming in the stomachs of nursing animals and infants are formed by rennin or hydrochloric acid has been studied and solved by A. KREIDL and A. NEUMANN (*Zentralbl. f. Physiol.*, 1908, xxii, 133) by means of the ultramicroscope. Casein clots produced by the action of acids could be seen by the ultramicroscope to return to their original fine emulsion before dissolving, when sodium hydrate was added; the clots produced through coagulation with rennin were dissolved by the alkali without returning to this stage. Milk clots from the stomach of nursing animals, as well as clots from the stomach of an infant fed with cow's milk, were dissolved directly by the rennin, thus showing that in all probability the milk in the nursing infant's stomach is clotted by the rennin and not the hydrochloric acid. That the same is true of human milk is more than probable, as the infant's stomach contains active rennin, and is acid in reaction, and it has been shown in vitro that human milk is coagulated by rennin.

**An Analysis of 500 Cases of Spinal Infantile Paralysis.**—J. COLLINS and T. H. ROMEISER (*Jour. Amer. Med. Assoc.*, 1908, i, 1766) present, in tabulated form, the analysis of 500 cases of spinal infantile paralysis, 327 of which they observed during the epidemic of 1907 and 173 previous to it. There were 297 males and 203 females; 311 developed in the months of July, August, and September; 62 were less than one year old, 158 between one and two years, and 134 between two and three years, thus showing that by far the greater number are less than three years old. High fever was noted in 145, slight fever in 191, no fever in 29; in 261 patients it lasted less than four days; in 100 more than four days. Vomiting was recorded in 151, anorexia in 78, diarrhoea in 49, constipation in 88, retention in 37, incontinence in 5, somnolence in 87, stupor in 40, unconsciousness in 10, rigidity and retraction in 56, insomnia and restless in 34, twitching in 66, convulsions in 18, delirium in 18, screaming in 32, crying in 59, and immotility in 59. One leg was paralyzed in 216, both legs in 134; in 65 the lumbar and gluteal muscles; in 36 one arm and in 5 both; in 35 cranial nerves were affected; 32 had quadriplegia, 27 triplegia, in 29 the abdomen and diaphragm and in the same number the neck muscles, in 20 the back muscles, in 15 the rectus oculi, in 14 the larynx and tongue, in 9 the facial muscles and also those of the chest, in 6 the sphincters, and in 3 the pharynx. The lumbar enlargement is oftenest affected, next the cervical and then the dorsal, not infrequently also the bulbar structures. The diaphragm was paralyzed only once. Trauma was noted very rarely as a preceding factor; most of the children previously were in the best of health; the paralysis was usually noted two to four days after the onset of the disease. Both ascending and descending Landry types of paralysis were observed. The infection finds the entire central nervous system and its coverings susceptible. A considerable number of their patients made a fair recovery.

## OBSTETRICS.

UNDER THE CHARGE OF

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**Prolapse of the Normally Situated Placenta.**—STERN (*Monats. f. Geb. u. Gynäk.*, 1908, xxvii) reports the interesting case of a patient in her ninth pregnancy. Previous pregnancies had all been terminated by artificial help. There was no history as to the course of the third stage of labor in these cases. The present pregnancy had proceeded without disturbance. There was no sign of hemorrhage whatever. Stern was summoned to the patient by a midwife, because spontaneous labor had ceased. On examination the abdomen was greatly distended. The amniotic liquid was excessive in amount. The foetus was small. The heart sounds were very faintly heard, and the foetus occupied a transverse position. Uterine contractions were strong and there was no hemorrhage. On internal examination the cervix was completely dilated, the membranes unruptured and tense, and no evidence could be found of the placenta. An effort was made to turn the child internally, but this failed. The membranes were ruptured between the pains and the hand introduced to perform version. As soon as the membranes were ruptured a very strong pain developed, which closed the cervix so that but two fingers could be inserted. The amniotic liquid escaped freely, although the hand and arm were used as a plug to prevent its entire loss. As the last of the fluid escaped it was noticed that it was blood tinged. The uterus relaxed after the membranes were ruptured, and the finger on entering the cervix found the placenta. As the hand was introduced the entire placenta was found lying detached at the internal os. The child was immediately turned and extracted, and although it breathed a few times it did not survive. The placenta issued from the uterus without uterine contractions as soon as the head of the child escaped. The placenta was entire and there was no large retroplacental blood clot. The membranes had ruptured about 10 cm. from the border of the placenta, which was one of the points against placenta prævia. Examination of the body of the child showed death from asphyxia. These cases are to be distinguished from placenta prævia in its various forms, accidental separation of the normally implanted placenta accompanied by hemorrhage. In the present instance there was no hemorrhage either before, after, or during labor, and the placenta could not be found on internal examination until the cervix was completely dilated and the child was about to emerge. In the case cited the occurrence of polyhydramnios had undoubtedly something to do with the prolapse of the placenta. The sudden and great change in the intra-uterine tension following the escape of the amniotic liquid, may have been largely instrumental in the prolapse. As a predisposing cause of this accident one must recognize the abnormal conditions in the endometrium and the decidua, which are so frequently seen in placenta prævia.

**Chorio-epithelioma, with Metastasis in the Vagina.**—BRENNER (*Monats. f. Geburts. u. Gynäk.*, 1908, xxvii) concludes an interesting paper upon this subject. The case which he describes had never belonged in the category of cases of beginning typical malignant chorio-epithelioma, and arose from the proliferation of villi following the development of vesicular mole. The growth of the syncytium and its proliferated cells occurred in Langhans' layer; the wandering cells of the chorion arose from both Langhans' layer and the syncytium. This could be demonstrated in the case reported. The development of the placenta seemed to be normal, but elements partly placental and partly foreign seemed to develop in the chorio-epithelioma. The character of the growth was essentially malignant, and its predominating feature was the rapid dissemination of syncytium. The degree of malignancy seems to depend upon the development of tissue in the tumor and tissue in the maternal organism as well. It is practically impossible to differentiate between the two. It is not yet clearly established that the syncytium arises from the chorion only; it may develop in part from the maternal tissue; in both epithelial and endothelial tissues are concerned. In the matter of diagnosis and prognosis the histological study of a given tumor is most important. When the tissues about the tumor are involved, operation should be preferably done by the vaginal route.

**Extirpation of the Uterus for Difficult Labor following Vaginal Fixation.**—ROSTHORN (*Monats. f. Geburts. u. Gynäk.*, 1908, xxvii) reports the case of a multipara who, two years previous to coming to the hospital, had vaginal fixation of the uterus done. During pregnancy there was great distention in the pelvic veins and those of the lower extremities. There was also disturbance in the function of the bladder. Labor developed very feebly and abnormally; the foetus was in transverse position; the uterus enormously enlarged transversely, and there was no possibility for spontaneous labor. In endeavoring to introduce an elastic bag to dilate the cervix, the posterior vaginal wall, which was greatly stretched was ruptured; this was followed by very free hemorrhage which was controlled with difficulty by tampons. The abdomen was at once opened, the uterus opened, the child extracted, and the placenta removed. The posterior wall of the uterus was enormously distended and very thin; the anterior intra-uterine wall, over an area as large as the hand, was closely adherent to the vagina. A gauze tampon was used to shut off the abdominal cavity from the pelvis. The patient made a good recovery complicated by phlebitis in the lower extremity. On examining the uterus its contour had been completely altered and spontaneous labor, or even delivery by any method except section, would have been impossible.

**The Supports in Chief of the Female Pelvic Viscera.**—PARAMORE (*Jour. Obstet. and Gynec. Brit. Emp.*, June, 1908) reviews the literature of this subject and discusses the part played by intra-abdominal pressure and the levator ani muscle. He concludes that the pelvic viscera are maintained in their position by two sets of forces: The one acting from above pins the viscera in their position; this is the intra-abdominal pressure. The other from below supports the viscera and prevents them from being displaced by excessive force from above. These two forces

vary with each other; the increase of the one produces the increase of the other. Both of these factors are under the control of the nervous system. The most essential element in maintaining the normal visceral position is supplied by the levator ani muscle. During defecation the visceral connective tissue is capable of supporting the viscera temporarily, but it is not capable of more than this. When this muscle becomes insufficient the viscera prolapse after a time.

In the same Journal, Fothergill discusses the pathology and operative treatment of displacement of the pelvic viscera. He concludes that in cases of classical prolapse anterior colporrhaphy, with union in the middle line of the parametric and paravaginal tissues, is indicated; with this should be performed posterior colporrhaphy and closure of the perineum. Ventrofixation in patients in whom conception cannot occur is indicated in addition, if necessary. When cystocele and vaginal prolapse are present, anterior colporrhaphy and closure of the perineum and pelvic floor are indicated. When the uterus is persistently retroverted and movable Alexander's operation is indicated, and when the uterus is fixed, abdominal section should be performed, adhesions separated, diseased appendages removed, and the uterus secured in anteversion.

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**The Excretion of Creatinin in Puerperal Patients and its Relation to Involution of the Uterus.**—LONGRIDGE (*Jour. Obstet. and Gynec. Brit. Emp.*, June, 1908) made observations upon ten patients delivered in Queen Charlotte's Hospital, who had normal labors and recoveries. The patient's diet was regulated, consisting of milk, eggs, porridge, and bread and butter. The total nitrogen of the urine was estimated and the creatinin was determined by Folin's method. The percentage of nitrogen excreted as creatinin during the nine days following delivery varied from 4.2 on the first day to 3.2 on the ninth day. The average percentage for the whole puerperal period for creatinin is practically 3, which is the normal one for the excretion of endogenous creatinin. If creatinin is manufactured by muscular autolysis then its percentage should have been increased in these patients under the muscular exertion of labor. These results indicate that autolysis of the uterine muscle does not occur in normal cases. These results are in accord with those of Mellanby, who found in experiments in which bacteria were eliminated that creatin and creatinin are not produced by muscular contraction. The excretion of total nitrogen in these cases showed increase on the fifth and sixth days, and then decrease. During the first four days it varied but little. It seems rational to believe that this is the result of uterine involution. The uterus loses half its weight in normal involution during the first week, probably due to the comparative anemia of the uterus. This, however, is not entirely the result of anemia. Longridge believes that the development of sarcolactic acid in the uterine wall after delivery favors autolysis. After labor the uterus is left, if well contracted, in a comparatively anemic condition with diminished alkalinity. These two factors favor rapid autolysis. As the uterus becomes softer and the blood passes freely through it, it becomes alkaline, the products of autolysis are gradually removed, and its rate very much diminished. In rare cases, in which the patient loses blood greatly after labor, the uterus may undergo excessive involution and practically disappear.

## GYNECOLOGY

UNDER THE CHARGE OF

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**Early Tubal Gestation: A Clinical Study.**—A. C. HERMAN SUHR (*Jour. Obst. and Gyn., Brit. Empire*, 1908, xiii, 261) has carefully studied a series of 109 cases of early tubal gestation with special reference to operative and palliative treatment. Suhr states the present ideas on treatment are somewhat as follows: (1) There is a consensus of opinion with regard to the very serious cases, which show obvious signs of severe internal hemorrhage, that there is only one course open, namely, immediate laparotomy. Dispute is confined almost entirely to the various types of less serious cases, such as the following: (2) In women presenting sufficiently obvious signs of a serious condition, such as the formation of a pelvic hematocele, and having, as a rule, had several attacks of severe abdominal pain, the general opinion is now in favor of operation without unnecessary delay, and Suhr says the experience of this series will show that this opinion is justified. (3) There is another type of case in which the treatment is perhaps most in dispute. These are cases in which the signs and symptoms are slight or have occurred some time before the patient comes under observation. It is probable that the ovum has perished and that the risk is over. It is from these cases that the largest number is chosen for expectant treatment, a course which Suhr endeavors to show to be by no means free from danger. (4) There are cases in which the ovum has been retained for some considerable time. Even in such cases there is evidence that there is danger in leaving them to nature.

To the 88 cases taken from the St. Thomas Hospital Reports by H. Bell, Suhr has added 21 he has minutely studied. Of the 21 but 17 cases were operated upon. No mortality ensued. Of the 109 cases 13 were left alone and recovered and 3 died after operation. Vaginal section was done 6 times, and is not recommended; 90 cases were subjected to abdominal section (80 primarily and 10 secondarily) with 3 deaths.

In several the foetus was found living at operation a number of weeks after the first symptoms of rupture. In one case the patient was kept under observation three months when urgent operation was required. The deaths were in two instances the result of curettage and infection of the hematocele under a wrong diagnosis before section was made, and in the other from operation for uncontrollable hemorrhage in a case under observation in the hospital. Suhr believes that there can be no question that cases with signs of severe internal hemorrhage require immediate operation and that we are not at present qualified to select our cases, and until we are able to do so with certainty it is best to operate. He lays particular stress on the point that in but one case in which only abdominal section was the treatment did death occur. It

might be added that in that instance the delay of the operation incident to palliative treatment is probably responsible for the fatal ending. He states a change in methods shown by the newer series (21 cases) is the complete demise of vaginal section as a method of operative procedure. As a primary operative method it has shown itself to be dangerous and useless, and has recently been employed only as a method of drainage. Suhr's paper is ended by these conclusions: (1) The tendency toward more frequent operation is justified and the results are much improved; (2) the risk of abdominal section is not greater than the risk of leaving cases without operation, and (3) we are at present unqualified to select with safety cases for expectant treatment.

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**Two Cases of Multilocular Retroperitoneal Cysts in Women.**—ALBERT DORAN (*Jour. Obstet. and Gyn., Brit. Empire.*, 1908, xii, 257) mentions 2 cases, one in a girl aged fifteen years, and the other in a woman aged thirty-nine years. Both were situated on the left side and extended from the pelvis to the ribs. In one the descending colon was on the outer side, and in the other in front of the tumor. Large bloodvessels passed from the mesenteries to the capsule in each instance. The kidney was behind the tumor in each case and the adrenal had no apparent relation to the tumors. Neither had a pedicle. The cyst walls were very thin and the contained fluid was clear and thin. The cyst wall was found to be made up of almost pure fibrous tissue without any adrenal, glandular, sarcomatous, or carcinomatous elements. They are believed to have developed from the Wolffian bodies. One has had no recurrence in the subsequent twenty-two years and the other for a number of years.

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**The Occurrence of Ovarian Tumors in Sisters.**—A. C. BUTLER-SMYTHE (*Jour. Obst. and Gyn., Brit. Empire*, 1908, xiii, 266) records three instances of this character in which he operated on the six patients. In each instance one sister was single and the other married. In the first the unmarried sister had two large multilocular cysts; the other a large multilocular cyst and a large cystic ovary. In the second each sister had a dermoid tumor of the left ovary. In the third each sister had a multilocular tumor of the right ovary and both patients were said to be pregnant. In all three instances the sisters from each family were operated on consecutively. All of the patients came under notice within the period of sexual life.

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**Fistula between the Fundus of the Uterus and the Upper Portion of the Intestine.**—WILLIAM F. GRAVES (*Amer. Jour. Obst.*, 1908, lvii, 353) reports a case of this kind that occurred in a woman, aged thirty-eight years. Graves had first seen the patient six weeks after she had been delivered instrumentally of a dead child, at which time the uterus was supposed to have been ruptured, a loop of intestines removed through the uterus, and a constant fecal discharge through the vagina resulting. Abdominal section made May 24, 1907, revealed a mass of intestine matted together in the left side of the pelvis by adhesions which were thoroughly freed with little damage to the bowel wall. The intestine,



less than two feet from the duodenum, had been severed completely. The upper end of the jejunum passed directly into the upper portion of the left broad ligament and was attached clearly to the uterus just below the left horn. It was adherent to the uterus and the cavities of these two organs connected through an aperture 2 c.c. in diameter. The lower segment was completely sealed above by adhesions to the wall of the false pelvis several inches away from the end of the upper segment. Intestinal anastomosis with closure of the fistula was successful.

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**High Rectocele after Perineal Repair.**—R. L. DICKINSON (*Amer. Jour. Obst.*, 1908, lvii, 347) in discussing this subject says the factors in the production of rectocele seem to be: (1) Laceration or lack of tone in the fascia and muscles of the pelvic floor. (2) Injury to the muscular layers of the rectal wall, or defective activity of such layers. (3) Defects in conformation of the rectum, or in the axis of the rectal canal, or of the anal canal or both. (4) Obstruction from vigor or irritability of the sphincter. Dickinson comments on the unreliability of post-mortem observations on the configuration and tonicity of the rectal and anal canal and on the falsification due to the relaxation from anesthesia. His methods of study upon the conscious subject are: (1) The rectum is distended with air and viewed with specula, either in the knee-chest posture or the lithotomy position with the head lowered; (2) by digital touch; and (3) by tracing tape or wire, the resultant measurements and angles being plotted on a full-sized sketch. Special points are noted by specular and digital examinations, and by means of the lead tape or solder wire running from the pubic crest to the sacrum with little slides on it which are placed at the coccyx, anus, fourchette, and crest of the rectocele, a tracing is made which together with the rectal examinations afford data for a definite appreciation of the injury to the rectovaginal partition. To prevent high rectocele, after repair of perineal injuries, it is necessary to make a digital rectal examination of the septum without general anesthesia; to identify the structures properly at operation, and to institute a very systematic after-care of the patient. This last precaution Dickinson considers highly important.

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**Voluminous Multilocular Ovarian Cyst in a Woman Aged Seventy-three Years.**—A DELETREZ (*Ann. de gyn. et d'obst.*, 1908, v, 231) has recorded a case of this disease in which he removed the tumor, weighing eighty-eight pounds, the contents of which were colloid in character. The tumor had ruptured spontaneously before operation. The patient recovered sufficiently to leave the hospital eighteen days after the operation.

## OPHTHALMOLOGY.

UNDER THE CHARGE OF

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**Oculopalpebral Epithelioma; Accidental Cure of Blindness.**—DUJARDIN (*Clin. Ophthal.* No. 8, 1908, p. 119) reports a remarkable case in which a large epithelioma beginning at the margin of the lower lid and extending across the entire cornea completely concealing it with, of course, total blindness of the eye. Immediately upon striking his head accidentally against a tree the affected eye received a violent contusion with profuse hemorrhage. When this was arrested the man found that he had recovered his sight. The cornea was found entirely uncovered and intact and the remains of the tumor formed a thick fringe about the lower border on the nasal side. Instead of forming an integral part of the cornea the tumor was evidently simply superimposed upon that membrane which retained its transparency intact. A few similar cases have been previously reported. It may therefore be advisable, in tumor of the anterior segment of the eyeball, to make a careful dissection to determine the condition of the subjacent cornea.

**When Glasses are not to be Prescribed.**—JACKSON (*Amer. Jour. Ophthal.* January, 1908, i) urges that glasses are not to be prescribed under the following conditions: (1) When there is no ametropia or eyestrain. (2) When ametropia is present, but does not limit the power of vision, or cause discomfort, or harm of any kind. (3) If the symptoms present, although such as are likely to rise from ametropia are probably due to other causes. (4) In the case of eyestrain connected with imbalance of the ocular muscles, it is too frequently expected that spectacles will give relief. Sometimes they do; sometimes they are a necessary adjuvant to other treatment. But in a large proportion of cases the fault lies in the central nervous system, the general nutrition of the patient, or his habits of life. (5) Spectacles should not be prescribed without an accurate knowledge of the error of refraction to be corrected. Of the ten thousand combinations that might be made from the trial case 9990 would not give any relief. The system will take drugs poured into it and dispose of them in some way usually without serious ill effects in a short time; but the effects of glasses for good or ill continue so long as they are worn. (6) Colored glasses are only indicated for some temporary purpose and not for permanent hypersensitiveness as to light. The latter is an indication for rest of the eye.

**Defect of Abduction Associated with Retraction of the Globe in Adduction.**—GREEN'S (*Ophthalmic Record*, February, 1908, 62) case presented all the features typical of the syndrome as laid down by Duane: that is,

partial absence of outward movement, partial deficiency of inward movement, retraction of the globe in adduction, a sharply oblique movement up and in and down and in, in adduction, paresis of convergence, and narrowing of the palpebral fissure. The absence of adduction probably indicates that the externus is replaced by an inextensible cord. The restriction of adduction may be due to inability of the normally inserted internus from exerting its full function with an inelastic externus or the internus may be inserted too far back on the globe, its function being inefficiently assumed by the superior and inferior recti. The recession of the eyeball into the orbit is explained by some to be due to the hugging of the globe between the inelastic externus and the contracting internus; by others to the oblique line of pull of the superior and inferior recti. The oblique movements observed in adduction are believed by Duane to be due to spasmodic action of the inferior or superior oblique, probably often combined with spasm of the superior or inferior rectus. Much uncertainty exists as to the cause of the narrowing of the palpebral fissure; Harman ascribes this simply to falling in of the lids from loss of their natural support when the globe is retracted. The insufficiency of convergence appears to be due to mechanical hampering of the internus. Tenotomy is hardly justifiable, while advancement is contra-indicated. Duane was able to collect 54 instances of this condition, of which 6 were observed by himself, whence it is probable that it is less rare than appears, being at times overlooked or incorrectly interpreted.

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**Osteoma of the Orbit.**—BIRCH-HIRSCHFELD (*Clin. Ophthal.*, No. 19, 1907, p. 286) reports three operations for osteoma of the orbit, of which one resulted in death. Unoperated osteoma is far from benign as some believe. The risk if unoperated is greater than when the tumor is removed. The operative dangers can be lessened by early diagnosis, rapidity of technique (injury of the base is especially to be avoided), and by treatment of the inflammatory affections of the frontal sinus which frequently accompany the growth. Microscopic preparations from these cases showed that ossification is, as in the normal bone, endochondral and perichondral and periosteal, and not solely periosteal as has been stated.

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**Family Nystagmus.**—In Apert's and Dubosc's cases (*Ophthalmoscope*, September, 1907, 399) a family of 10 children, 4 by the first husband and 6 by a second, all of the latter were affected with nystagmus without evidence of ocular or general disease, except that in three of the children the knee jerks were exaggerated. The father was dyspeptic, had always been subject to violent migraine, neuralgia, and pain. His mother had suffered from temporary auditory hallucinations. Of the 4 children by the first marriage, 3 unaffected children were dead, while one, aged thirteen years, had no nystagmus, but was affected with fibrillary twitchings of the muscles of the lips, especially the upper, coming on every two or three minutes. The reporters think that their cases were instances of myoclonic nystagmus of the hereditary-familial variety described by Lenoble and Aubineau.

## **PATHOLOGY AND BACTERIOLOGY.**

UNDER THE CHARGE OF

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**The Coronary Arteries of the Human Heart.**—MERKEL (*Verhandl. der deut. path. Gesell.*, 1907, 10th Tagung., 127) in trying to explain the lack of lesions in the myocardium in a case in which the left coronary artery was occluded has devised a very ingenious method of studying the distribution of the coronary arteries. The vessels are injected with red lead, mixed preferably with gelatin. The heart is hardened in formalin, and later is skiagraphed by a method which permits of the examination of the picture with a Bartholdy stereoscope. Of particular interest was the blood supply of the septum. To the anterior portion of the ventricular septum the left coronary furnishes large and numerous branches, while to the posterior half go smaller twigs from the circumflex branch of the right coronary. Under normal conditions communicating branches were found in the septum between these vessels. Anastomoses were likewise observed in the auricular septum. In hypertrophy of the heart an astonishing increase in the vascularity of the heart was found; the right coronary artery entered into this in a slight degree, but it was principally noticeable in the branches of the left artery. In certain cases extremely large vessels anastomosed in the ventricular septum, even when there were no anastomoses on the surface of the heart. The author believes this is significant in explaining the occurrence and the absence of myocardial lesions following disease of the coronary arteries.

**The Relationship of the Neighboring Vessels to Angiomas of the Skin.**—A. OPPENHEIM (*Frankfurter Zeit. f. Path.*, 1907, i, 124) injected into a freshly excised nevus a solution of Berlin blue. The piece of tissue was first dipped into paraffin to prevent the escape of the solution from the open ends of the vessels of the subcutaneous tissue. Thick sections were then cut and studied with the microstereoscope. By this means it could be determined that the normal bloodvessels of the surrounding subcutaneous tissue connected directly with angioma. At the base of the angioma the bloodvessels, which formed the tumor, were of their usual size, but toward the surface they branched out like the cords of a whip, became unusually wide, and formed coils.

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All communications should be addressed to—

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THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES.

OCTOBER, 1908.

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ORIGINAL ARTICLES.

**A CLINICAL STUDY OF SOME ARRHYTHMIAS OF THE HEART.**

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THE last few years have seen many important changes in the point of view of physicians toward disease of the heart. Not only have new and important physiological facts been discovered, but there is an increasing tendency on the part of practising physicians to make use of them. Notably is this the case in regard to the anatomy and physiology of the atrioventricular bundle. Moreover, the recent work of Mackenzie, Wenckebach, Hering, Cushing, Engelmann, Hoffmann, Minkowski, and a host of others upon the general subject of arrhythmia has opened up an entirely new field in the pathology of the diseases of the heart, and makes it desirable that the diseases of the circulation generally should be studied from the new standpoint, and by the aid of the new methods which these investigations have introduced. A large amount of work has been expended upon the study of the extrasystole, and this feature of arrhythmia seems destined to become more and more prominent, so that its bearings upon clinical medicine will need to be much more clearly and definitely defined than is at present possible.

Unfortunately, physiologists are still far from being in accord as to the exact origin and meaning of the various types of extrasystoles, and even a definition of the term has not been universally accepted. Probably the most satisfactory definition yet offered is that of Mackenzie,<sup>1</sup> who says: "I would suggest that the term extrasystole

<sup>1</sup> Quart. Jour. Med., 1907, i, 137.

should be limited to those premature contractions of the auricle or ventricle in response to a stimulus from some other portion of the heart (than the normal), but where otherwise the fundamental or series rhythm of the heart is maintained."

The present paper is concerned with an effort to define more clearly than is usually done the purely clinical relation of the terms Stokes-Adams syndrome, heart block, and extrasystole to one another, and especially through the study of two cases to attempt to throw a little light upon certain clinical problems that are not very infrequently met with in connection with disorders, organic or functional, of the bundle of His.

Although it is but a few years since the anatomy of the atrio-ventricular bundle has been known and its function all but established, the literature of the subject, especially upon its clinical side, has already reached large dimensions, and each week brings a fresh group of reports of cases.

The number of cases with satisfactory autopsical reports of the condition of the heart is still, however, rather small, especially of cases in which there has been an opportunity during life of studying the physiology of the circulation by the more modern methods, especially by satisfactory combined radial and jugular pulse tracings.

A study of recent reports of clinical cases, moreover, suggests that the exact relation of the terms Stokes-Adams syndrome, heart block, bradycardia, and extrasystole, from a clinical standpoint, have not been quite clearly established, that these conditions are not always recognized and differentiated, and that the terms are not in every case employed accurately. The great complexity of the subject, together with the fact that physiologists are still far from being in accord as to the genesis of many of the cardiac arrhythmias, makes it seem likely that it will be long before the whole subject of arrhythmia is made clear; in the meantime it is hoped that the report of carefully studied cases of these types of heart disturbance with their curves, diagrams, and lesions, may ultimately help to clear up this important field.

Gibson<sup>2</sup> has collected fourteen cases of heart block with postmortem examination of the heart, including one case of his own, and the literature of these cases is referred to in his article. Of these, the following are the lesions described as involving the bundle of His:

	Cases.
Tumor . . . . .	2
A mass, nature not stated . . . . .	1
Stretching and obliterating of bundle . . . . .	1
Atheroma . . . . .	2
New interstitial tissue . . . . .	5
Gumma . . . . .	1
Fatty degeneration . . . . .	1
Anemic necrosis . . . . .	1

<sup>2</sup> Quart. Jour. Med., 1907, i, No. 2.

For the details of these cases the reader is referred to Gibson's paper.

A case that seems to have escaped the notice of Gibson was published by Rendu.<sup>3</sup> There was marked bradycardia, with pulse of 30 to 40, and with jugular pulsation not synchronous with the apex impulse. The autopsy showed a gumma in the auriculoventricular area, together with well-marked fibroid changes in the ventricular septum.

Since Gibson's paper, in January, 1907, the following additional cases have been reported: Ashton, Norris, and Lavenson<sup>4</sup> report a case of complete heart block with a gummatous deposit involving the bundle of His. The continuity of the bundle is said to have been destroyed. Butler<sup>5</sup> reports a case of typical complete heart block, with fatty infiltration of the bundle of His. Vaquez and Esmein<sup>6</sup> report a case of Stokes-Adams disease, bradycardia with attacks of syncope. The autopsy showed double aortic disease with a patch of sclerosis corresponding to the position of the bundle of His. Microscopical study also showed destruction of the bundle. Deneke<sup>7</sup> reports three cases of heart block studied clinically and with autopsies. In Case I there was found a gumma involving the bundle; in Case II the heart was unfortunately lost. Case III showed fibrous degeneration of the bundle. Dock<sup>8</sup> reports a case of partial heart block due to fibroid changes in the endocardium over the left branch of the bundle of His, also involving the bundle. It is possible that still other reports may have escaped my notice.

The first of the two cases with which the present paper is concerned was one of complete acute heart block from a destructive lesion involving the atrioventricular bundle at the node.

CASE I.—A male, aged sixty-five years, married, came first under observation on July 28, 1907. There was no history of lues nor of alcoholism. He had never had rheumatism, but forty years ago had an attack of malaria, following which a systolic murmur was found at the apex of the heart. This murmur has persisted, and its existence was well known to him for many years. At no time in his life had he noticed any symptoms of cardiac insufficiency, and the heart lesion had never caused him the slightest inconvenience. He was an exceptionally vigorous and active man both physically and mentally. About seven weeks ago, having been in perfect health, he began to show signs of fatigue on slight exertion and to feel feverish sensations. There was also slight headache. At times he was confused and forgetful. He soon developed a low grade of fever, with slight mental confusion, but no other symptoms. One week ago his confusion and forgetfulness increased, but he was rational when addressed. At this time the temperature was 102°. Two days ago

<sup>3</sup> Soc. méd. des Hôp., 1895.

<sup>5</sup> *Ibid.*, cxxxiii, p. 715.

<sup>7</sup> Münch. med. Woch., 1907, liv, 1101.

<sup>4</sup> AMER. JOUR. MED. SCI., January, 1907.

<sup>6</sup> Presse méd., 1907, xv, 57.

<sup>8</sup> Brit. Med. Jour., 1907, 1039.

there was numbness in the left leg. Examination showed an elderly man of large frame, well nourished and well preserved. The mental processes and speech were somewhat slow, but in other respects normal. There was a visible pulsation in the neck above the clavicle, the rate of which was about double the cardiac rhythm as indicated by the pulse and by the heart sounds. Examination of the heart was as follows: The cardiac impulse was in the fifth space, seven inches to the left of the middle line. It was both visible and palpable, and was strong but slightly irregular. The area of dulness extended seven inches to the left of the middle line. The right border of dulness was normal. At the apex there was heard a loud blowing systolic murmur, musical toward its close, transmitted to the left to the axillary line, and heard also over the entire precordium. The pulmonary second sound was feeble. The action of the heart was very slow and deliberate and slightly irregular. There was heard a very faint sound between each two heart beats, a sound of indefinite character. This was plainest over the base of the heart, and was believed to represent an auricular systole. The lungs and abdomen were normal. The pulse was somewhat irregular in force and frequency, slow, deliberate, of fair fulness, moderate force, normal tension. The vessel wall was markedly thickened. The pulse rate varied between 32 and 40. The extremities were normal. The Babinsky and Oppenheim phenomena were present on the left side. Power and sensation were normal. There was no rash and no petechiæ. The examination of the urine was as follows: Amber color, 1020 specific gravity, no sugar, a faint trace of albumin, a few hyaline and granular casts. There were five examinations of the urine at intervals, all of which gave approximately the same result.

The patient's condition remained unchanged for ten days, when the dulness and apathy became more marked. The fever varied from 99° to 104°, pursuing an irregular course, and at no time falling to normal. There was but one chill, on August 17. The pulse rate varied from 32 to 40, as a rule, occasionally reaching 50. The respirations varied from 24 to 32, but became more rapid toward the end. The apathy grew deeper, and he could be roused with great difficulty. On August 20 he died.

The temperature curve (Fig. 1) is reproduced as offering an opportunity of studying the influence of an active toxemia upon the heart's action in heart block. The leukocytes varied from 12,300 on admission to 28,700 a few days before death. The differential count showed: Polymorphonuclear neutrophils, 81.5 per cent.; lymphocytes, 18; mononuclear cells, 1. Culture of the blood showed a pure growth of a very slowly growing *Streptococcus pyogenes*.

Simultaneous tracings were taken from the radial artery and the jugular vein from time to time, in some cases the Jaquet chronosphygmograph being used, and in others a large Zimmermann kymograph with Verdin-Marey tambours and a Jaquet chrono-

graph registering fifths of a second. In the latter tracings a Marey transmission sphygmograph was applied to the radial artery, and a Mackenzie cup to the jugular vein. The sphygmogram in every case shows the entire absence of any lesser intermediate beat corresponding to the feeble intermediate heart sound above described (Fig. 2). The radial strokes are uniform in force and regular in rhythm. The jugular tracings show complete dissociation of the auricle from the ventricle. The *C* wave can in every case be clearly made out, occupying its exact and proper time relation to each radial

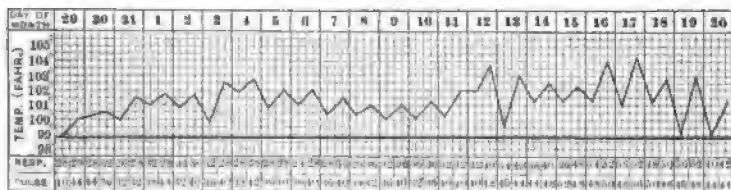


FIG. 1.—The temperature, pulse, and respiration in Case I.

stroke, while the *A* waves are somewhat more than twice as numerous, are equidistant from one another, and occasionally almost coincide with *C* waves, but the two sets of waves bear no definite relation to one another. The temperature chart shows that, contrary to what has been sometimes stated, the inherent rhythmical rate of the ventricles is influenced by the toxemia, but not in proportion to the influence that is exerted upon the auricular rate. An interesting and remarkable phenomenon is noticed in the terminal stage, in that at times the rate of the pulse is actually lower than that of the respiration.

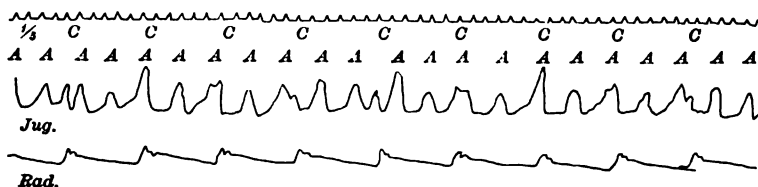


FIG. 2.—Tracing from Case I, showing complete heart block.

The association of complete heart block with the symptoms and signs of malignant endocarditis led to the conclusion that there was an ulcer on the interventricular septum immediately beneath the undefended space.

The summary of the autopsy report is as follows: Lungs, congestion and edema, with a small healed focus of tuberculosis at the right apex. Liver, moderately enlarged and pale. Spleen, normal. Kidneys, of normal size, firm, capsule adherent, surface rough and nodular. Cortex thinned, markings indistinct. Chronic diffuse

nephritis, interstitial type. Pericardium, normal. Heart, markedly increased in size, the increase affecting both the left and right ventricles and the auricles.

The great vessels were tied off with the heart in situ. The organ was then removed, its cavities distended with formalin, and opened after hardening in such a way as to present the same view of the organ that is given in Tawara's monograph. The mitral valves are markedly thickened, and are the seat of several large, smooth polypoid vegetations. At the anterior line of union of the two cusps is an area of recent ulceration. On the interventricular septum immediately beneath and posterior to the undefended space is a large ragged ulcer measuring 3 x 1.5 cm. and 1 cm. in depth (Fig. 3). The ulcer has a very irregular outline and a ragged base, upon which more or less thrombus is deposited. The ulcer reaches out to and is continuous with the ulcerated surface just at the junction of the two leaves of the mitral valve. When compared with the photograph and diagram of the human heart in Tawara's monograph,<sup>9</sup> it is seen that the ulcer must completely destroy the atrioventricular bundle at the level of the node. The specimen was not cut up for microscopical study, as it seemed to show the lesion more clearly and positively macroscopically than it could possibly do under the microscope. This specimen seems to show a more positive and complete destruction of the bundle of His than does any other with which I am acquainted.

In this case there was complete heart block, as shown by tracings and by the autopsy, but without the Stokes-Adams syndrome, there being only bradycardia with extra jugular pulsations, but at no time either syncopal or epileptoid seizures. To be sure, the patient while under observation, was always in bed, but other cases of Stokes-Adams disease frequently show convulsions when quiet in bed, and this patient had been going about, travelling abroad so recently before his death, as to make it seem fairly certain, considering the lesion, that the heart block had been present before his taking to bed, and always without any such seizure.

The second case with which this report is concerned is one which shows a typical Stokes-Adams syndrome, in that there is bradycardia with a pulse rate of 30, visible and palpable pulsations in the jugular vein, together with cerebral seizures, sudden faintness with partial loss of consciousness, complete syncope or convulsions, but in whom there is good reason to believe that atrioventricular conductivity is at all times perfect.

CASE II.—J. S., aged fifty-five years, a cook, came under observation suffering from fainting attacks with palpitation of the heart. His family history is good, and throws no light upon the trouble. He has lived in New York for seven years, and has been generally

<sup>9</sup> Das Reizleitungssystem des Säugetierherzens, Jena, 1906.



**FIG. 3.**—Interior of the left ventricle of Case I showing a ragged ulcer on the interventricular septum immediately beneath the undefended space.





healthy. He has taken tea, claret, and beer in moderate excess until of recent years, since when he has taken but little. He had malaria at the age of six, cholera at nineteen, and typhoid fever at twenty-seven. He has never had inflammatory rheumatism. He has had urethritis several times. Twenty years ago he had a venereal sore of five days' duration, and four years later a second, but there have been no secondary symptoms. He has had urethral stricture for fifteen years.

*Present Trouble.* For about fifteen years he has noticed shortness of breath and feelings of cardiac oppression upon exertion. Four years ago he had an attack of dizziness; he was taken to a hospital, and was told that he had heart trouble. Thereafter he remained well until July, 1907, since which time he has been subject to dizzy attacks, at first once or twice a month, and for the past three months much more often, and recently of daily occurrence, sometimes as many as from three to ten a day. Two weeks ago he had about twenty in one day. He knows no cause for these.

With the attacks he may or may not have palpitation of the heart. In the last three days he has had no attack. There has been no oedema; there have been no urinary symptoms excepting those due to stricture; no pain over the heart, but some dull, aching pain in the lumbar region. He has lost about twenty pounds in the last three months. Examination shows a rather poorly nourished man, slightly cyanotic, somewhat prostrated, and with a look of illness. No dyspnoea. The radial pulsations are equal, but bear very little relation to the cardiac impulse, about half as many beats reaching the wrist as occur at the apex. The pulse is of fair size and good force, the vessel wall diffusely thickened. The lungs show a few subcrepitant rales at both bases behind, more marked on the right side. The liver and spleen are normal; the abdomen is normal. The cardiac impulse is visible and palpable in the fifth space 11.5 cm. to the left of the middle line. By percussion the left border at the fifth space is 13 cm. to the left of the middle line; the right, at the fourth space, is 4 cm. to the right of the middle line. The cardiohepatic angle is normal. The heart's action is regular. There are sixteen forcible apex impulses to the half minute, and regularly interpolated between these are sixteen lesser beats. This rhythm continues for a certain length of time, and then is succeeded by a fairly regular series of beats of equal size and force. This continues for a few minutes, and the regular rhythm is resumed, 60 to 64 per minute. There is a pulsation of large amplitude in the great vessels of the neck which at times bears no relation to the apex impulse. There is a faint systolic murmur at the apex heard with the loudest beats, but not heard with those of less intensity. The systolic murmur at the base is loudest in the aortic area. The extremities are normal. The patient's condition for the next two weeks remained about the same; the pulse was at times from 30 to 36, and at other

times from 60 to 70 per minute. The patient feels well, and is up and about. He has had three slight attacks of dizziness but no syncope. Fluoroscopic examination of the heart showed a rather small excursion of the left border. The right border showed a sudden rounded expansion due apparently to the filling of the auricle, but the examination was not satisfactory enough to establish whether dissociation of auricles and ventricles was present or not.

March 31. For fifteen seconds there were seven beats at the wrist, being at the rate of 28 per minute, but in the following twelve seconds there were 17 beats at the wrist, at the rate of 85 per minute.

April 6. At 5.30 P.M. he began to feel dizzy; this was followed shortly by a paroxysm of tachycardia. The heart rate was from 204 to 250. There was a well-marked cardiac impulse in the fifth space 11.5 cm. to the left of the middle line, and another, almost as well marked, in the sixth space 14 cm. to the left. With the attack there was a feeling of weakness and oppression beneath the sternum. He vomited several times and was relieved. He thought the tachycardia was brought on by walking up and down stairs to test his heart.

April 10. He has been perfectly well for three days. This morning while being examined he suddenly complained of feeling dizzy; his eyes became expressionless; for a period of half a minute his condition was analogous to the momentary staring and loss of consciousness of petit mal. During this period the heart passed through a series of irregular contractions, and then settled down to a perfectly regular tachycardia at 220 per minute, this lasting five minutes and stopping suddenly. After the dizziness passed off the only discomfort was the palpitation and sense of oppression just above the sternum.

The history of the attacks as obtained from the patient is as follows: "The exciting cause of these attacks of syncope and tachycardia, which have come as often as twenty in one day and been absent as long as twenty-six days in one stretch, cannot be determined. Many times he is wakened from his sleep by dizziness, to become unconscious and have a typical attack. Again, a slight exertion, as walking, going upstairs, or straining to pass water, may be followed by an attack. But these same exertions, or even more severe ones, at another time may have no harmful effect. The attack comes on suddenly with dizziness, grayness before the eyes, and a buzzing in the head like an organ. There are no premonitory symptoms. Unconsciousness follows rapidly, and when he comes to, the heart is beating very rapidly (200 to 260 a minute), there is a choking sensation, as if a ball were in the throat, and he is shaking all over. There is never any pain over the heart or down the arm. At times he has been struck down as if 'by electricity' without warning; again, he has simply had the dizziness, grayness, and buzzing without loss of consciousness, but with tachycardia succeeding very quickly. The tachycardia lasts a varying length of time, sometimes for only ten

minutes, at others all day.' During its continuance he has great gastric distress, with frequent vomiting. He has noticed that the more severe and sudden the onset, the longer the tachycardia persists. He cannot forecast the end of the attack until it is at hand. Then, at times, the violent regular beating of the heart is succeeded by two or three irregular beats, 'as if something shook the heart,' and this is immediately followed by two or three tremendous throbs of the heart, with each one of which there is a feeling as if fresh air were forced into his throat and head, and the attack stops as suddenly as it began. But it stops permanently only when there have been three big beats. If there are only two big beats, it stops for a few seconds or minutes only, and is then off again in another violent beating, to last until three big beats put an end to the attack.

The irregular beats, coming just before the terminal large ones, are not constant; sometimes he has them, sometimes not. The three terminal, heaving thrusts of the heart are succeeded by the usual normal slow heart action, the choking sensation and vomiting cease, and he feels perfectly well again."

April 24. He has had repeated short attacks of tachycardia which have not been affected by medication. Between these attacks the pulse is always perfectly regular, the rate being sometimes 30, sometimes 60, the transition from the one rate to the other being absolutely sudden. Thus, the only paroxysm of tachycardia which began while the patient was under observation was immediately preceded by a short period of irregular, infrequent pulse beats, during which there was dizziness and loss of consciousness. The patient himself recognizes the paroxysms of tachycardia by the symptoms which accompany these phenomena, and he also recognizes periods of intermission of the pulse when the pulse rate is about 30; these latter give rise to sensations of varying degrees of unpleasantness, from a simple sinking feeling to what he describes as a series of heavy shocks passing up the neck and through the head and, at times, through the whole body, as if—in his words—"air was being blown through his head and body." With this there is often dizziness and a slight loss of consciousness. During the tachycardia also he sometimes loses consciousness, and at times also he has slight convulsions.

A careful study of the physical signs shows that when the pulse is 60 the heart rate is absolutely regular both in force and in rhythm, both heart sounds being fairly clear and distinct. With the 30 rate the pulse also is entirely regular and of somewhat greater amplitude than during the 60 rate. Over the apex and the base of the heart during the 30 rate there are heard a loud first sound and second sound, followed, after a very brief interval, by a heart sound which is sometimes single and sometimes double, then a comparatively long, presumably compensatory pause, and a full heart sound, this alternation or bigeminal character being regularly continuous for a variable length of time. No radial pulse can be felt corresponding

to the smaller alternating heart sounds, nor can a cardiac impulse generally be felt at this time, although, as will be seen by reference to the tracings, a small impulse can be registered by the cardiograph. But coincident with this there is a very marked pulsation in the neck, both visible and palpable, and this pulsation is of far greater amplitude than any other that is felt. If the hand is placed in the supra-clavicular fossa so that the fingers cover the external jugular vein, their tips resting upon the innominate artery, it can be positively determined that, whereas the regular full heart beats can be felt in the innominate, but without a corresponding jugular pulsation, with the extrasystole the innominate pulsation disappears and the jugular pulsation becomes of great amplitude.

A study of coincident radial, jugular, and apical tracings shows conclusively that the phenomenon is one of extrasystole, and it can be proved by reference to the tracings that these extrasystoles, occurring with great regularity and between each two normal heart beats, occur so soon after the physiological systole that they are unable to open the aortic valve, and so fail to be effective by forcing blood into the aorta. This failure is dependent upon their early occurrence after the systole, and is due to three physiological conditions: (1) The systole itself is feeble by reason of coming so soon after the last refractory phase; (2) the blood pressure in the aorta is still very high; and (3) the ventricle contains but little blood.

For discussion and analysis of the varieties and origin of extrasystole the reader is referred to the writings of Cushing,<sup>10</sup> Mackenzie,<sup>11</sup> Wenckebach,<sup>12</sup> Hering,<sup>13</sup> Ortner,<sup>14</sup> Hoffman,<sup>15</sup> Hirschfelder and Eyster,<sup>16</sup> and others.

The jugular tracings of many of the cases of heart block and other heart maladies that have been published are not as convincing as the average careful reader could wish, but the tracings of this case appear to be especially clear and to demonstrate many of the events normal and abnormal that can be read in pulse and vein curves, and so they seem to justify publication and discussion.

Beginning with the cardiogram in Fig. 4, the sudden upstroke with the slight rounded eminence is generally supposed to mark the sudden filling of the ventricle by the auricular contraction;<sup>17</sup> we then find the usual systolic plateau gradually falling to the base line, and so giving a perfectly normal cardiogram.

In the jugular tracing we find a wave marked *A*, due to the systole of the auricle; this wave begins about  $\frac{1}{40}$  second before the cardiac impulse. After an interval of  $\frac{1}{2}$  second, the normal period, the

<sup>10</sup> Trans. Assoc. Amer. Phys., 1899, xiv, 172.

<sup>11</sup> Arrhythmia of the Heart, Edinburgh, 1904.

<sup>12</sup> Verh. d. Cong. f. inn. Med., 1906, xxiii.

<sup>13</sup> Deut. Arch. f. klin. Med., Band lxxviii, 39; Deut. Klin., 1903, p. 155.

<sup>14</sup> Amer. Jour. Phys., 1907, xviii, 222.

<sup>15</sup> Wenckebach, Arrhythmia, p. 50.

<sup>16</sup> Quart. Jour. Med., i, No. 1, 39.

<sup>17</sup> Ibid, 1907, 424.

*C* wave occurs, marking the carotid impulse derived from the underlying carotid artery. The position of this wave enables us to establish a definite period in the jugular pulse, whether we agree with Mackenzie that it is always produced by the carotid artery, or with Hering,<sup>18</sup> who believes that it may be produced also by other agencies. In the radial tracing the radial pulse is seen to occur  $\frac{1}{10}$  second after the carotid pulse. In the jugular tracing, immediately after the *C* wave, are seen two smaller waves, the latter of which is with some of the beats of considerable magnitude. The meaning of the former is not clear, but the latter is probably the *V* wave marking the passive filling of the auricle, before the opening of the tricuspid valves, and followed by a rapid fall coincident with the opening of these and the rapid emptying of the auricle into the ventricle. Following this is the largest wave seen, marked *X*. This is synchronous with the quick, strong jugular pulsation, which is both visible and

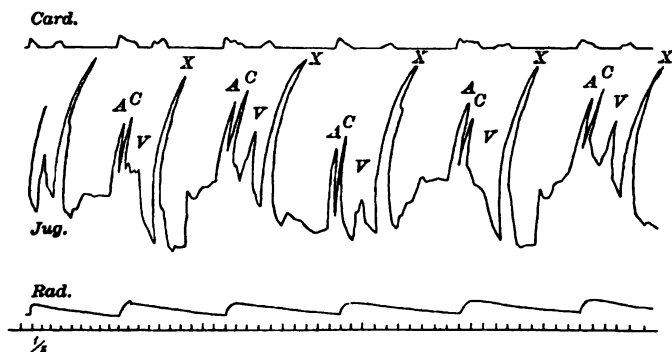


FIG. 4.—Tracing from Case II, showing extrasystoles, simulating heart block.

palpable, and which occurs in the interval between two pulse beats, but nearer to the one that precedes it than to the one which follows it. This was at first supposed to mark an auricular systole which did not reach the ventricle, and, therefore, to indicate heart block, but it is associated with a cardiac impulse, as shown by the cardiogram. Moreover, if the distance between the beginnings of these two cardiographic impulses is carefully measured, it is found that this *X* wave corresponds exactly in point of time to the ventricular, and not to the auricular systole, and so must be regarded as an extrasystole, ventricular in time, and not preceded by the usual auricular wave. The origin of the stimulus to this extrasystole is probably in the atrioventricular bundle, and not in either the auricle or the ventricle, for the following reasons: It cannot be auricular, (1) because there is no evidence of a wave at the time when such an auricular systole

would naturally make a wave, that is,  $\frac{1}{2}$  second before the extraventricular systole; and (2) because the corresponding cardiogram in every case fails to show any auricular rise, such as is present in each of the alternate cardiograms.

It cannot be ventricular, (1) because, as is shown in other tracings in which the pulse rate of 30 alternates with that of 60, the intermission is distinctly less than two normal heart beats (Cushing, Hering, and others), although it must be remembered that Hirschfelder claims that this is not a safe criterion for the ventricular origin of extrasystole; and (2) because there is no sign in the tracing of what would be the next regular auricular systole midway between the two waves marked *A*, that is, of a lost auricular systole.

For all of these reasons it is evident that *X* is an extrasystole whose stimulus has its origin in the atrioventricular bundle, a stimulus which is propagated in both directions and brings about at the same instant a systolic contraction of both auricle and ventricle, thus corresponding to the type of extrasystole described by Mackenzie.<sup>19</sup> The unusual amplitude of this wave *X* is to be explained on two grounds: (1) There is a simultaneous systole of both the auricle and the ventricle; and (2) the ventricular systole follows so close upon the preceding full systole that at the time of its occurrence aortic pressure is so high that it is unable to open the aortic; and presumably also the pulmonary valves, thus failing to give rise to a radial or innominate pulse, but blowing back through the incompetent tricuspid valve, thus giving rise to this extraordinary wave.

In occasional tracings from this patient a very slight elevation of the line of the sphygmogram is seen, coinciding with the *X* wave, showing that at times the aortic valves are lifted to a slight extent.

It will be observed that there is generally a notch to be seen on the descending limb of the *X* wave. This is probably due to and marks the time of the closure of the pulmonary valves, indicating, when present, that right ventricular pressure has been sufficiently raised to open these valves. It will also be noticed that this notch, probably a pulmonary dirotic notch, occurs at the lowest point on those *X* waves that follow *V* waves of the least amplitude, and that are preceded by the most rapid and extensive depressions. This probably indicates that with these heart beats the tricuspid valves open early and a larger amount of blood than usual rushes into the ventricle, enabling it to throw more blood into the pulmonary artery.

In Fig. 5, which shows the 60 pulse rate suddenly changing to the 30 rate, with the immediate appearance of the *X* wave, it is noticed that in the first long interval a very slight elevation appears in the sphygmogram, indicating that the aortic valves opened, and some blood was thrown into the aorta, and at the same time it is seen that the corresponding *X* wave is much smaller than those which follow,

<sup>19</sup> Quart. Jour. Med., 1907, i, 131.

and has a more marked dirotic notch, which may be taken as indicating that the pulmonary valves, too, open fairly freely, leaving less blood to be blown back through the tricuspid orifice.

Fig. 6 is a tracing from the same patient during a paroxysm of tachycardia, the rate being 210. It is seen that the rhythm, as shown

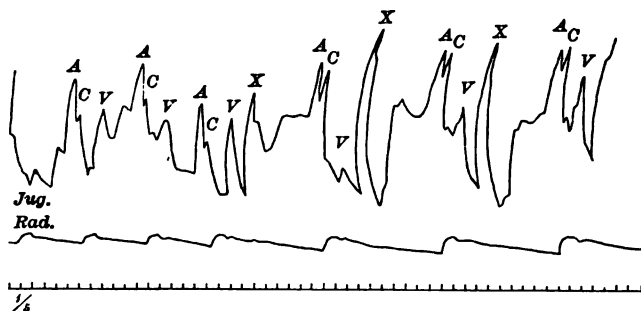


FIG. 5.—Tracing from Case II, showing sudden change from normal to slow pulse rate with extrasystoles.

by both cardiogram and phlebogram, is perfectly regular. The jugular tracing shows a jugular pulsation occurring  $\frac{1}{6}$  second before each cardiac impulse. This shows that the right auricle contracts before the ventricle, and stamps the tachycardia as one having its stimulus from the auricle or from the mouth of the great veins, not from the node or from the ventricle.

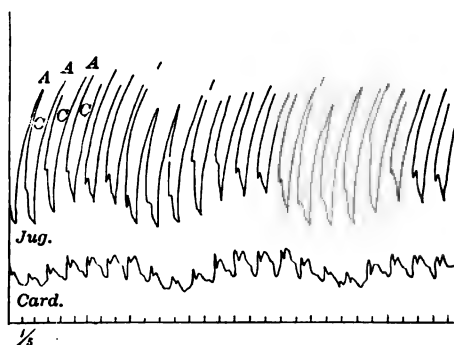


FIG. 6.—Tracing from Case II during tachycardia.

If Hoffmann's theory is correct, that paroxysmal tachycardia is virtually tetanus of the heart, a contraction being set up as soon as the organ emerges from the refractory period, by reason of a constantly present stimulus, then the refractory period of such a heart could be estimated mathematically by dividing sixty seconds by the pulse rate per minute. This, carried out in the present case, gives a refractory period of 0.285 second, while the rate is 210. If this period

is laid out on the jugular tracing, Fig. 2, it is seen that the wave *X* regularly occurs at a considerable period after the heart has emerged from its refractory phase, and that, therefore, presumably the origin of the extrasystole is different from that of the tachycardial systoles, as was already indicated by a study of the tracings.

One may fairly conclude that this patient possesses an atrioventricular bundle that is abnormally irritated, or that develops stimulus material abnormally, and that it exhibits three phases of atrioventricular rhythmicity: (1) A phase when stimuli develop at the normal rate and in the normal situation, and when the heart beats regularly and at 60 to 64 per minute. (2) A phase of extrasystole when the atrioventricular node is abnormally active, and when the extrasystoles thus produced bring about a condition of arrhythmia which simulates heart block. (3) A phase during which the auricular portion of the bundle is the seat of such constant stimulus production that the heart beats regularly at 210. These very rapid beats are not extrasystoles, but abnormally rapid physiological systoles, for their origin and transmission are normal, their only abnormal feature being the rapidity with which they follow one another. It is noted also that a well-defined auricular rise is present in the cardiogram during tachycardia, indicating that the sequence of events in the heart systole is then normal.

These two cases, then, show three distinct abnormalities of the atrioventricular bundle: (1) A destructive lesion of the bundle at the node; (2) an abnormal irritability or rhythmicity at the node; and (3) a similar abnormal rhythmicity at the sino-auricular junction.

I believe from my own experience, as well as from a study of the cases of heart block reported by others, that certain cases of regularly recurring extrasystole simulate heart block and have been so recorded. This is a point to which writers upon this topic, Mackenzie, Wenckebach, Hering, and others, have already called attention, but the point probably deserves to be called more directly to the notice of physicians, especially as the clinical significance and prognosis in these two sets of cases are entirely different. The prognosis in heart block is generally bad, but in extrasystole it is generally much less grave.

I have also observed another case, in a woman, aged sixty-five years, who suffered from chronic diffuse nephritis and chronic myocarditis; the pulse at the time she was seen was beating regularly and continuously at 48 per minute; the heart systoles, however, were 95 per minute, and each alternating one followed closely the preceding systole, as could be determined by auscultation, and the same phenomenon that has been just described could be felt in the neck; that is, an unusually forcible venous pulsation accompanying the extrasystole, but without either a radial pulse or a discoverable pulsation in the innominate artery. In other words, it was a case of extrasystole simulating heart block. This method of examination



by simultaneous palpation of the innominate artery and the jugular vein is of considerable service in making this differentiation.

A second case of alternating slow pulse and paroxysmal tachycardia is now under my observation, in an overworked business man, aged forty-two years, who since boyhood has experienced abnormal sensations in the precordium, referred by him back to a severe muscular overstrain. His symptoms are almost identical with those of the patient S. There is moderate enlargement of the heart to the left, with short systolic murmur at the apex, transmitted a short distance toward the axilla. Generally the pulse is absolutely regular and of normal frequency. At times there is tachycardia of sudden onset, frequent occurrence, generally brief duration, and terminating with one, two, or three very forcible beats. At other times there are regularly recurring extrasystoles giving a radial pulse of 36, with heart beats of 72 of the true bigeminal type. None of these extrasystoles reach the wrist; with the slow pulse is a sensation of sinking, or, as the patient describes it, like a sudden descent in a swift elevator, and at times incomplete loss of consciousness. Both varieties of arrhythmia are brought on by the same causes, sometimes by active exercise, but more often and more certainly by writing.

These cases suggest the possibility that such bradycardia simulating heart block is more frequent than is generally supposed.

In conclusion, the above cases show: (1) That complete heart block going on to a fatal termination is possible without the Stokes-Adams syndrome being present at any time; (2) that complete Stokes-Adams syndrome may exist in the presence of perfect atrio-ventricular conduction, an example of which condition has also been mentioned by Lepine;<sup>20</sup> and (3) that there is another and closely allied syndrome consisting of tachycardia in the presence of mitral and tricuspid regurgitation, associated with syncopal and epileptiform seizures.

The physiological end result of these conditions is the same as in the Stokes-Adams syndrome, in that many systoles are lost through their being unable to open the aortic valves, while the physiological origin is entirely different, being in the one case hyper-rhythmicity of the atrioventricular bundle, and in the other, a blocking of this structure.

I acknowledge much assistance from Dr. Stuart Hart in obtaining and studying the various tracings.

<sup>20</sup> Sem. méd., December 18, 1907.

# SUBTEMPORAL DECOMPRESSION IN A CASE OF CHRONIC NEPHRITIS WITH UREMIA; WITH ESPECIAL CONSIDERATION OF THE NEURORETINAL LESION.

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AND

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THE patient, Mrs. B. S., aged twenty-two years, was admitted to Dr. Barker's service in the Johns Hopkins Hospital,<sup>1</sup> on July 24, 1907, complaining of headache and vomiting, pain in the joints, and swelling of the legs. Her father died with some obscure cardiac symptoms. . . . With the exception of chronic indigestion and "sick headaches," from which she has suffered off and on all her life, she has always regarded herself as reasonably well and strong, until her present illness. She had diphtheria when twelve years of age, but knows of no other infectious diseases. She was married a year ago; has never been pregnant. She has lived a very unhygienic life, standing at work in a factory for long hours, six days in the week.

The present illness is said to have begun abruptly, five weeks before her admission, with a persistent headache for which there was no determinable cause. (It is probable from her history of dyspepsia and headache that the trouble had been of long standing.) One week ago swelling of the feet was first noticed; she has had pains in her arms and legs for the past four days, and has been unable to retain anything on her stomach. Heretofore she has vomited occasionally, but only in association with her sick headaches.

*On admission:* the patient is a dark complexioned, young woman of slender build, and sparsely nourished. Her buccal and conjunctival mucous membranes are pale. . . . The left pupil is slightly larger than the right. Both react normally to light and accommodation. . . . Both eyes are slightly prominent, the right more than the left; v. Graefe's and Joffroy's signs are positive; Stelwag's sign is absent. Convergence is a little weak in the right eye. The thyroid gland is not palpably enlarged. Her chest is fairly well formed; . . . respiration is clear without adventitious sounds. The point of maximum impulse of the heart is visible in

<sup>1</sup> We wish to express our indebtedness to Prof. L. F. Barker for the privilege of using the notes here abstracted from the patient's medical history; to Dr. G. R. Henry, of the medical staff, for her careful record of the case and unflagging devotion to the patient; to Dr. W. G. MacCallum and Dr. Winternits, of the pathological department, for the autopsy report and sections of the eyes; to Dr. Frederick H. Verhoeff, of the Massachusetts Charitable Eye and Ear Infirmary, for his aid in the study of the retinal lesion; and to Mr. Louis Brown, of the Massachusetts General Hospital, for the excellent photomicrographs of the sections.

the fifth interspace 7 cm. from the midsternal line. . . . Relative cardiac dullness . . . considerably increased. At the apex a rough blow, which is transmitted to the base and can be heard over the auricular area, follows the first sound. The aortic sound is ringing and amphoric; . . . the pulmonic second sound is greatly accentuated, and a soft systolic blow is heard over the pulmonic area. The radial pulse is 80, regular in force and rhythm; the vessel is palpable. Systolic pressure equals 175 mm. of Hg. The abdomen is negative. There is no enlargement of the liver. . . . There is no oedema of the extremities; the platellar reflex is equal on the two sides and very active. There is a leukocytosis of 14,800; the blood is otherwise negative. The urine is pale yellow in color; specific gravity, 1012; no sugar; a trace of albumin and flocculent sediment containing hyaline and granular casts. Albumin, 0.5 gram to the liter; urea, 12 grams to the liter. The subsequent twenty-four hour amounts varied from 510 to 1200 c.c.

On July 27 the patient complained of pain in her right knee, which was held flexed and appeared swollen; . . . an accumulation of fluid in the joint associated with tenderness. . . . On the following day there was a similar complaint of discomfort in the left shoulder; . . . she had had recurring attacks of discomfort of this kind before her admission.

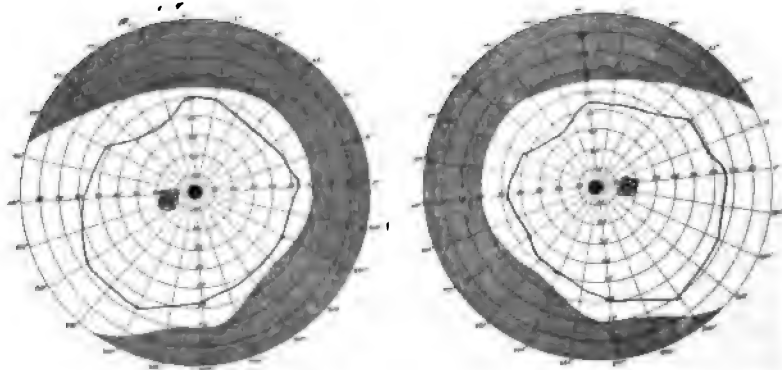
On July 30 she suffered from an exceedingly severe headache, moaning constantly, and occasionally crying out with pain. There was considerable mental confusion at times, . . . and periods of dullness during which it would be difficult to arouse her. . . . Her systolic pressure registered above, 230 and the second aortic sound was extremely loud and ringing. A sweat bath was given, but this so disturbed her cardiac action that it had to be interrupted; . . . she perspired freely, however, and the measure seemed to give some relief.

*Ophthalmoscopic Examination* (Bordley). "Media are clear; pupillary reflexes are normal. There is a swelling of the right disk of 6 D., of the left of 7 D. The disks are very cedematous; the outlines are entirely lost; the physiological cup is filled in; the larger veins and arteries are seen dipping in and out of the extreme oedema both over the disk and adjoining retina. There are a great many small hemorrhages on the disk and on the retina near it. There is no stellate figure in the macula, and at this distance from the disk there is little swelling of the retina. The retinal picture of the two sides is practically the same." Vision =  $\frac{20}{200}$  right eye;  $\frac{10}{200}$  left eye. There is a concentric contraction of the field of vision with an enlarged blind spot (Figs. 1 and 2). Impossible to make color tests owing to patient's exhausted physical condition.

From this time on until October 24, the time of her operation the history may be condensed as follows (the notes are taken from numerous detailed observations made by Drs. Fletcher, Emerson,

Morris, Sladen, Beall, Henry, and others of the medical staff who had her under observation during these three months):

She continued in very much the same state described above, having occasional days of improvement, but for the most part suffering from severe headaches, nausea and vomiting, and other signs of pressure. The notes upon her cardiac condition did not vary greatly, although occasionally a diastolic murmur could be heard loudest at the apex and traceable as far as the anterior axillary line. The systolic murmur remained audible. A capillary pulse was occasionally observed in her finger nails. There was a more or less constant elevation of temperature during the first weeks after her admission, ranging from  $100^{\circ}$  to  $103^{\circ}$ . This occurred in association with the swelling of the joints, although at no time was there any evidence of a suppurative arthritis. By a month after her admission anasarca was quite marked. The face was considerably swollen.



FIGS. 1 AND 2.—Visual fields charted July 30, 1907, showing slight constriction with enlarged blind spot.

During August she suffered greatly from pyorrhœa alveolaris, and at one time a dirty, grayish slough, starting from an ulceration of the gums, spread over the soft palate and inner surface of the right cheek. . . . Under energetic treatment this condition gradually improved.

She first began to complain of dimness of vision in September. (An ophthalmoscopic examination on September 13 is recorded as showing "intense albuminuric retinitis.") She seemed, however, subjectively somewhat improved, and early in October she was allowed for a few consecutive days to be out of bed and on her feet for some hours. . . . This resulted in accentuating her headaches and in producing marked swelling of her extremities, so that she again had to be kept recumbent. Subsequent to this there was a marked diminution in her visual cavity.

*Ophthalmological Notes, October 11 (Bordley).* "The palpebral orifices are wide. Slight exophthalmos of both eyes, probably more marked on the left. Upper lids definitely pigmented. Some slight fulness below the brows and loss of the associated movement of brow and superior rectus. No wrinkling of the brow. Involuntary spasmodic movement of upper lids when she looks upward. Upper lids at times are drawn above the corneæ sufficiently to expose the scleræ. There is loss of power of binocular convergence. The act of winking is incomplete, although not diminished in frequency. The lids close incompletely, and the effort brings out a marked tremor. It is difficult to evert the upper lids, particularly the right. The left pupil is slightly larger than the right; both of nearly normal size. The media are perfectly clear. The fundi present a peculiar appearance; the entire retina on both sides is so swollen that it is impossible to locate the disks. It requires a 5 D lens to see the surface of the retinæ distinctly. There remains no landmark by which the disk can be located. The whole surface of the retina is covered with hemorrhages of varying size and with tremendous yellowish white exudates. Two veins can be made out in each eye, but the other vessels are concealed. A careful search over the entire surface of both retinæ fails to disclose any signs of an artery. The picture is a most unusual one, and the changes since July 30 are astounding."

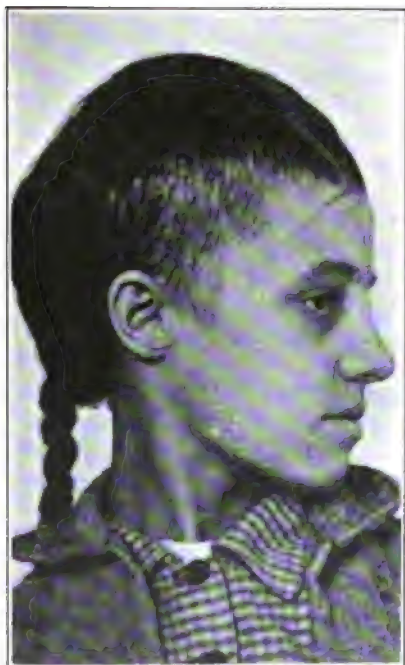
Later in October her symptoms became much aggravated, and definite signs of uremia appeared. A number of lumbar punctures were made during this period, in the hope of relieving some of her severe pressure symptoms. Fluid was always found under great tension, but its removal seemed to give no subjective or objective evidence of benefit—in fact, it usually had a temporary disturbing effect.

On frequent examinations the urine showed very little change from the condition noted at the time of her entrance. . . . The blood pressure remained high, its systolic level averaging from 200 to 250 mm., the diastolic level from 170 to 190 mm. Neither the lumbar punctures, nitroglycerin, nor other measures which had been tried had had any appreciable effect in lowering her high tension pulse.

In the light of some experiences in other renal cases in which notable temporary improvement in the general symptoms, as well as in the condition of the eyes, had occurred after lumbar puncture, we were led to suggest—owing not only to the advancing change in the eye-grounds, but also to her condition of semicomatose—the propriety of a decompressive operation, and the patient was transferred to the surgical side for this purpose.

*Operation, October 24, 1907. Right Subtemporal Decompressive Craniectomy.* Under chloroform anesthesia, with a curvilinear skin incision, the usual circular cranial defect with opening of the

dura was made under the right temporal muscle (Figs. 3 and 4). Owing to the fact that there was a large temporal muscle which could be readily elevated after splitting its fibers, the removal of bone was easily accomplished. The only difficulty which was experienced lay in the unusual degree of bleeding from all of the tissues, scalp, muscles, and particularly from the surface of the dura. The veins were considerably congested, and the arteries encountered were markedly tortuous and sclerotic. The dura was exceedingly tense, and, owing to the marked degree of cerebral protrusion which



FIGS. 3 and 4.—Photographs taken three weeks after right subtemporal decompression for the cerebral edema of nephritis. Note the curvilinear scalp incision and partial shaving of the head (Fig. 3), which allowed of subsequent concealment of the operative field with the patient's hair (Fig. 4).

followed the first incision, it was opened with some hesitation in the absence of a coincident lumbar puncture. It was accomplished, however, without injury to the pia arachnoid. The subdural space contained no free fluid. The arachnoid, on the other hand, was markedly distended with fluid, which escaped after pricking the membrane in a number of non-vascular spaces where it bridged the exposed sulci. Not only was there a superabundance of fluid in the arachnoid spaces, but the brain itself appeared soggy and wet. . . . The muscle, galea, and scalp were closed without a drain.

During the operation the systolic blood pressure fell from 300 to 210 mm. Hg.

The wound healed by primary union. Her general condition seemed considerably improved, although for some days she remained noisy, excited, and hysterical. Her headaches subsided; there was no further nausea and vomiting; her stupor rapidly disappeared; the usual lethargic state, even on her best days, was replaced by a normal mental activity.

*October 28, Ophthalmoscopic Examination (Bordley).* "Rendered difficult owing to the now contracted pupils, but it is evident that the swelling is distinctly less than before the operation. The situation of the disks can be clearly made out."

*November 4.* The patient was transferred again to the medical side. On this date the following note (Bordley) was made upon the eye-grounds: "The swelling of the disks and retinae, approximately the same on the two sides, does not exceed 1 D. The retinal tissue is much clearer. In the right eye there are several long, thin hemorrhages; in the left eye there are three wide, flat ones. The disks are covered with exudates and new connective tissue. There is only a faint trace of the physiological cup, which is filled in. The four principal veins can be distinctly made out in both eyes, and there is a suspicion that two arteries in each eye are visible as small, white lines. In the left eye there is the typical star-shaped figure usually attributed to albuminuric retinitis. Throughout each retina there are silvery white patches. Exudates are no longer to be seen. There is a vast and rather unlooked-for improvement in the condition of both eyes."

*November 13, Ophthalmoscopic Examination (Bordley).* "There is a still further decrease in the swelling of both nerves and retinae; the decrease in the retinae is so great that it now requires a minus lens to make out the details. (At this examination the existence of myopia became apparent for the first time.) The stellate figures are rapidly disappearing; where the lines which composed them formerly were solid, they now present a beaded and broken appearance; where they formerly were fused, they are now separated by clear retinal tissue showing clumps of pigment. The bloodvessels are much more distinct, but it is still difficult to recognize any arteries. The general condition is much improved."

*December 3 (Bordley).* "The general retinal condition shows additional improvement in a further subsidence of the swelling in both eyes. While the outlines of the disks cannot as yet be seen, the large exudative mass over them is completely absorbed. The physiological cup can be located by the white mass of tissue within its normal confines. The nephritic white changes and stellate figures are gradually disappearing. The vessels can be distinctly seen entering the cup. The appearance, instead of being that of a snow-white mass, is distinctly red, from the fact that the color of

the choroid is becoming discernible. In the left eye there are two or three apparently new hemorrhages and some small ones which follow the radiating direction of the Müllerian fibers in the macular region (to be accounted for possibly by an acute upset with headache and vomiting which was apparently occasioned by the excitement of attending, somewhat against her will, a medical clinic on the preceding day). The vessels, including the arteries, can now all be seen with great distinctness; even the margins of the disks are discernible. The perivascular spaces are filled in with white connective tissue."

After the operation and during the patient's two weeks' residence in the surgical ward she improved greatly, although the condition of the urine remained unaltered and her blood pressure continued at almost as high a level as before. Due doubtless to the abeyance of pressure symptoms, her appetite improved; she gained considerably in weight; her color and general appearance changed markedly for the better. She was up and about the ward for a month before her discharge, having only one upset of any kind and that—a day's headache—was apparently attributable, as mentioned above, to the excitement of attending an amphytheatre clinic.

The protrusion at the seat of the bone defect, which had been considerable for a few weeks after the operation, gradually subsided, and the temporal muscle lay flat from then until the time of her discharge. Her general condition was so much improved that we were led to discuss the advisability of renal decapsulation, in the hope of improving the vascular condition of the kidneys, but the patient felt so well that she begged to return home, at least for the holiday season; and rather against advice, in consideration of her unfavorable home surroundings, she was permitted to do so.

The physical examination made just before her departure showed practically nothing new. The cardiac condition remained the same, showing the increased area of dulness with a ringing aortic second, although no murmurs were heard on this day of discharge. The lungs were clear; there was no oedema. The blood pressure registered 200. She was free from headache and nausea—in fact, better than she had been at any time since her admission.

On December 26, two weeks after her discharge, she was re-admitted to Dr. Barker's service in a semiconscious state. Nothing definite could be learned of her movements during the interval, nor of the length of time she had been ill.

The examination on re-admission showed a marked and exceedingly tense protrusion at the seat of the decompression, which had been flat at the time of her discharge. She could be aroused so as to answer a few simple questions, but would sink again into a lethargic state. There was an extraordinary degree of subcutaneous oedema, confined to the tissues of her face and neck.

Her eyes were protruding, and the oedematous lids could be only



partially closed; the right palpebral cleft was wider than the left. The œdema involved the conjunctivæ, and there were redundant folds about the cornea. The right pupil was smaller than the left; they both reacted sluggishly to light. When aroused the patient was unable to see objects, although there apparently was some light perception. There was no squint; tests of ocular movements were unsatisfactory. The tongue protruded in the mid-line; it was covered with a heavy white coat. The jaw was not deflected. She could not be persuaded to move her facial muscles, so that the presence or absence of palsy could not be made out.

The examination of the chest revealed practically the same condition recorded at the time of her previous admission, although the respiratory sounds were now everywhere accompanied by medium fine moist rales. There was no ascites or evidence of accumulation of fluid elsewhere; no œdema of the extremities. Reflexes of the upper extremities were not obtained. There was an active patellar response on the left; on the right it was barely obtainable. A flexor response (?) occurred to plantar stimulation on both sides.

During the next three or four days the œdema of the face increased greatly; it was more marked on the left side than on the right, supposedly due to the position of her head, for it was held persistently turned toward the left; the eyes became completely closed. On lumbar puncture a small amount of cerebrospinal fluid was obtained: it escaped slowly—a drop in four or five seconds. The needle was left inserted until an ounce was withdrawn. There was no improvement or other alteration in her condition as a result of this measure.

Her stupor gradually deepened, and after the first few days it was impossible to arouse her. There was at no time any slowing of the pulse. The temperature, which was normal on admission, gradually rose to 101° and over. There was incontinence of urine. It is recorded in the notes that she could “grasp with her right hand;” that she could “move her left arm;” that there was “no paralysis of the arms.” An attempt to examine the eyes on two successive occasions was unavailing, even after the administration of atropine, owing partly to the patient's restlessness and partly to the extreme œdema of the lids and conjunctivæ.

Her blood examination showed: Red blood corpuscles, 3,896,000; white blood corpuscles, 10,600; hemoglobin, 75 per cent. The differential count was within normal limits.

By January 3 she was unable to swallow, and on the following day Cheyne-Stokes respiration appeared in company with a weak and irregular pulse.

On January 6 a second lumbar puncture found fluid under great tension; an ounce and a half was removed, with a resultant softening of the tense protrusion at the seat of the decompression. No change in her general condition followed the withdrawal of this fluid.

On January 7 there was evidence of pulmonary involvement, with dulness in the axilla and over the right back. Coarse, moist rales were heard everywhere; the respiratory sounds in the lower right axilla were distant.

She died on the evening of January 8, two weeks after her admission, there being practically no alteration in the clinical picture which has been given.

Reading between the lines of her second clinical history, the copious notes of which have been but briefly abstracted here, it is apparent that the chief attention of the clinicians was drawn toward her cardiovascular and renal state, in the belief that her condition was due to a return of uremic symptoms, little suspicion being held that an apoplectic stroke had occurred. In all likelihood the presence of a cerebral extravasation was masked owing to the cerebral distention which was permitted at the seat of her former decompressive operation; and it is improbable that with an intact skull she could have lingered for so long a time in the presence of such a large hemorrhage as was found at autopsy.

AUTOPSY, January 9, 1908, 11.30 A.M. Dr. Winternitz.

ANATOMICAL DIAGNOSIS. Chronic diffuse nephritis (small, granular kidney); cerebral hemorrhage; arteriosclerosis; hypertrophy of the heart; chronic aortic and mitral endocarditis; decubitus ulcers; chronic splenic tumor; hyaline degeneration of arterioles of spleen; choked disk with retinal degenerative changes; chronic tuberculous broncholympadenitis; acute bronchopneumonia (bilateral).

The *body* is that of a white woman, 155 cm. in length, considerably emaciated; rigor mortis is not marked. Livor mortis is considerable in the dependent portions. . . . The conjunctivæ are markedly bulged out and wrinkled. Over the lower portion of each cornea there is an opacity about 5 mm. in width. . . . In the left temporal region there is a defect, . . . the site of an old craniotomy. Over the sacrum there is a large decubitus ulcer, . . . also a second small ulcer over the left great trochanter. . . . The subcutaneous fat is of a deep yellow color and small in amount. . . . The peritoneal surfaces seem everywhere smooth and glistening. There is no excess of fluid. . . . The liver extends 8 cm. below the ensiform cartilage. . . . There are a few adhesions about the spleen and liver. The pleural cavities contain about 400 c.c. of bloody fluid; they are free from adhesions. . . . The pericardial surfaces are everywhere smooth and glistening; the sac contains no excess of fluid. The *heart* is somewhat enlarged; weighs 320 grams. The epicardial surfaces are everywhere smooth and glistening. The coronary vessels are prominent and tortuous; yellow plaques can be seen through their walls. . . . The tricuspid valve, especially its middle cusp, is somewhat thickened. . . . but seems competent. . . . The mitral orifice admits two fingers; the valve is slightly thickened and opaque, especially at

its line of closure and attachment of the chordæ tendinæ. The left ventricle is markedly hypertrophied and contracted. The wall averages 2 cm., and in places measures over 24 mm. The musculature is very pale; . . . here and there it is flecked by irregular, slightly yellowish areas. The aortic valves are somewhat thickened, and the line of closure . . . is slightly granular in appearance. The base of the aorta as well as the anterior cusp of the mitral valve contain numerous yellowish subintimal thickenings. The coronary arteries are tortuous and thickened, showing everywhere on their walls heavy yellowish, opaque plaques. The *left lung* . . . is of a mottled color, . . . more congested at the posterior border, while the lower lobe is of a deep purple. . . . The bronchi contain some frothy fluid. . . . On section . . . here and there small dark elevated reddish brown spots which are firmer than the surrounding tissue and stand out as very slightly granular areas. . . . The lowest dependent portion of the lower lobe is collapsed, non-air-containing and of a deep reddish brown color. The *right lung* is slightly more voluminous than the left. There is a large lymph gland at the hilum, the centre of which contains a broken down, cheesy mass about 1 cm. in diameter. This gland rests directly upon the bronchus. . . . Otherwise, this lung resembles the left in every respect. The *spleen* is separated with some difficulty from the parietal wall. It measures 12.5 by 5.5 by 3.5 cm.; weighs 100 grams. The capsule . . . is slightly thickened throughout. It is fairly soft. . . . The Malpighian corpuscles are made out with considerable difficulty, and there seems to be a slight increase in fibrous tissue. The *stomach* contains . . . about 200 c.c. of rather cloudy green fluid. The mucosa is mottled everywhere with small, reddish brown areas. . . . The biliary and pancreatic ducts are patent. The *pancreatic* . . . lobulation is rather distinct, but not excessively prominent. . . . The islands of Langerhans are visible. The *liver* . . . weighs 1320 grams. . . . On section the lobulation is rather indistinct. The liver substance is very pale. There are small, opaque, yellowish areas surrounding the hepatic veins.

The *kidneys* together weigh 120 grams. The *left kidney* is small; measures 9.5 by 5 by 3.5 cm. The capsule, which is somewhat thickened, strips fairly readily, leaving an irregular granular surface. The renal surface is mottled, pale, yellowish gray in color, with the superficial stellate veins . . . prominent. On section the substance of the organ is very pale. The cortex, . . . pinker in color than the pyramids, is noticeably thin and irregular; in some places measuring 4 mm., in other places barely measuring 2 mm. The striations are much obscured; where they are made out they are irregular and tortuous. The glomeruli are not seen. The pyramids are paler than the cortex and surrounding them there is a more opaque, yellowish area. The vessels are slightly engorged, but in no

place are hemorrhages to be made out. The *right kidney* measures 9 by 4.5 by 3.5 cm. It is very similar to the left. The pyramids are slightly pinker in color and the striations are obscured.

The *adrenal cortex* is somewhat opaque, yellowish, and there is a central semitransparent gray area in the medulla. The *bladder*, *rectum*, *tubes*, *ovaries*, *uterus*, and *intestines* are normal. The *aorta* contains numerous yellowish, subintimal thickenings, especially around the orifices of the intercostal and splanchnic vessels. The *thyroid* is slightly enlarged, of a transparent yellowish color. On section the colloid seems to be in excess and the alveoli enlarged.



FIG. 5.—Showing the situation of the apoplectic clot.

. . . The *brain* is apparently enlarged; oedematous; convolutions flattened. . . . There is a 5 cm. circular protrusion at the seat of the cranial defect where *dura* is missing. The protrusion involves chiefly the outer aspect of the right temporal lobe. The *arachnoid* is not adherent to the overlying temporal muscle. The floor of the third ventricle bulges markedly, and on pressure considerable fluid escapes when it is incised. On incising the right hemisphere to open the lateral ventricle of that side; . . . a large clot is found, which lies lateral to and above the basal nuclei (Fig. 5). . . . This extends laterally to within 4 mm. of the surface of the brain. . . . The outline of this clot is irregular, . . . and it is

placed somewhat more anteriorly than the usual capsular clot. The clot is for the most part. . . . of a homogeneous, deep, brownish black color, but that immediately next to the brain tissue is of a lighter shade and is more friable. The area of hemorrhage measures approximately 10 by 4 cm. The left lateral ventricle is slightly dilated. . . . The endyma is normal.

*Histology. Heart:* The muscle fibres are definitely enlarged, as are also their nuclei. . . . *Lungs:* . . . The alveolar walls are congested, and in some places the alveoli contain serum, in others small numbers of red and white blood cells with few endothelial cells and small amounts of fibrin. The consolidation is not very marked. *Bronchial lymph glands:* Contain numerous softened and necrotic eosin-staining masses of tissue which are fairly well encapsulated by a wall of fibrous tissue. In one of these some calcareous material is found. *Thyroid:* An increase of colloid; acini appear somewhat enlarged, and epithelium in places is possibly higher than normal; no involution figures of epithelium are to be observed. *Spleen:* Capsule and trabeculae slightly thickened. . . . The Malpighian bodies are normal, but their arteries are thickened and show an eosin-staining, glassy-looking media. The walls of the venous spaces show a definite increase in fibrous tissue. *Liver:* The cells surrounding the hepatic vein are somewhat shrunken and contain a considerable amount of greenish brown pigment. . . . *Kidneys:* Capsule is thickened. Coarse bands of connective tissue run in everywhere from the surface, giving the organ a mottled appearance. There are areas rich in fibrous tissue, where the tubules, as well as the glomeruli, are either distorted or entirely obliterated, or . . . where the epithelium has been desquamated, alternating with areas where the tubules are dilated with granular detritus or with homogeneous staining casts or cellular debris. The epithelium of the tubules is low, granular, and shows varying amounts of fatty change. The glomeruli, as a rule, are fairly well preserved, in some places showing thickening of their capillary walls. The vessels, especially of the sclerosed areas, show considerable hyaline degeneration. . . . *Brain:* The cerebral tissue at the edge of the extravasation shows a ragged border lined with well-preserved red blood cells. All through this area in the surrounding brain tissue, phagocytes heavily laden with a golden pigment are seen. . . . Organization is beginning to take place in certain areas. . . .

*Examination of the Eyes.* The optic nerve with the entire eyeball were preserved in 4 per cent. formalin for a few days, after which windows were cut in the globe to allow of further penetration of hardening fluid. Sections through the centre of lens and disk show, on gross examination, 0.6 mm. swelling of the disk, the physiological cup being filled in with new tissue (Fig. 6). The vaginal sheath of the nerve is dilated and the subdural space nearly obliterated by

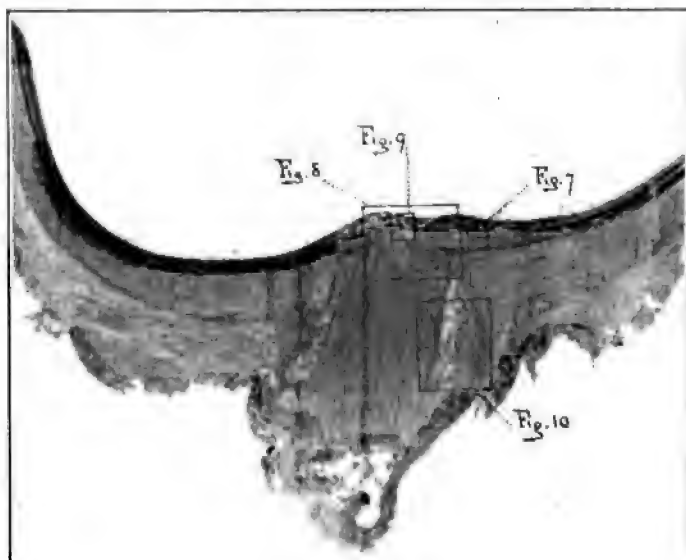


FIG. 6.—Microphotograph (6 diameters) of a section through the centre of the swollen disk and a portion of the optic nerve. The squares indicate areas from which subsequent figures have been taken.

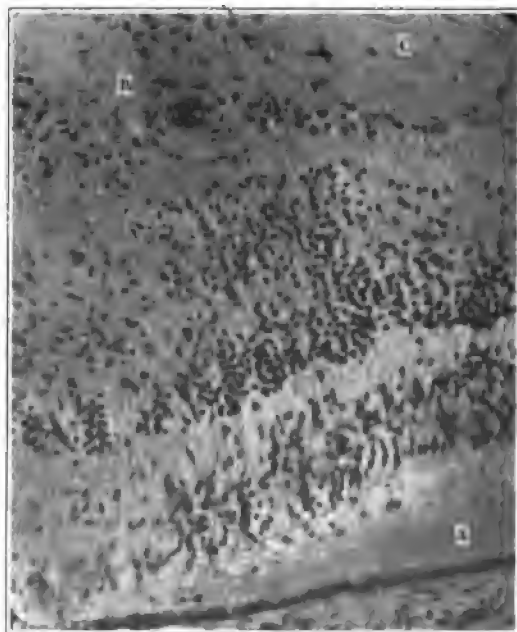


FIG. 7.—Showing A, retinal detachment; B, vessel containing hyaline thrombus; C, thickened nerve-fiber layer (200 diameters, reduced  $\frac{1}{4}$ ).

new tissue formation. The retinal separation is shown in several places by small, blister-like elevations (Fig. 7).

*Microscopically* there is loss of surface epithelium with round-cell infiltration in a small area of the right cornea; the anterior chamber is filled with leukocytes. In this eye there is hypopion keratitis. The other structures, exclusive of retina, choroid, and optic nerve, are normal. The following changes are present in each eye in practically equal degree:

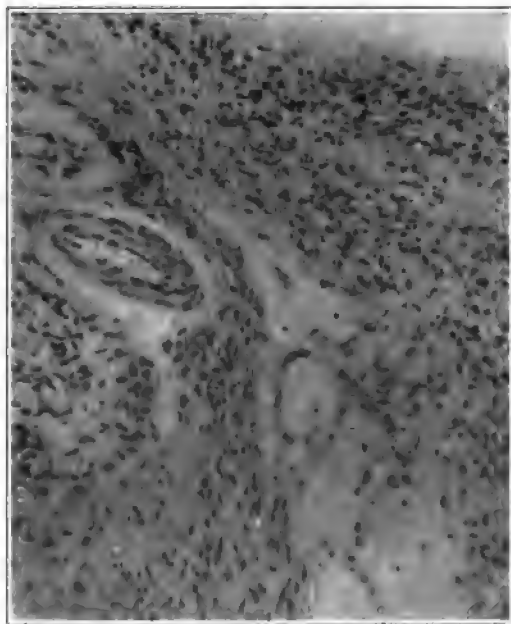


FIG. 8.—Showing the edge of the physiological cup filled with new tissue, subintimal thickening of vessels; vacuolated spaces, etc. (200 diameters, reduced  $\frac{1}{4}$ ).

*Retina.* Fairly large spaces in both the nuclear layers and the layer of Henle are filled with a fine meshwork, which appears to be of fibrin, judging from its affinity for eosin. There is marked proliferation of the neuroglia cells under the hyaloid membrane, giving the surface of the retina a wavy appearance. One large and several small retinal separations (Fig. 7) are visible, the spaces being filled with an albuminous coagulum. The multipolar ganglion cells are well preserved. The cytoplasm of some of the cells is shrunken; in others it is vacuolated, giving a swollen, transparent appearance to the cells. The nuclei show little evidence of degenerative change. The retinal vessels show distinct endothelial and subendothelial proliferation; in the perivascular lymph spaces, especially of the larger vessels, there is an increase in the connective

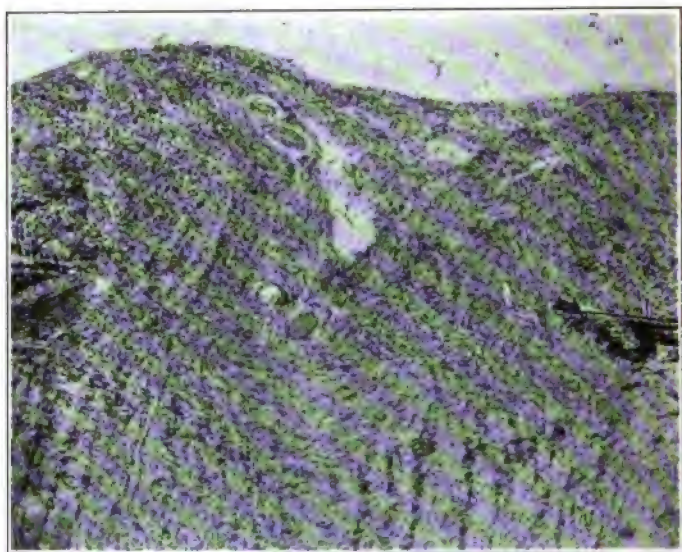


FIG. 9.—Showing the cup filled with new tissue; loss of the transverse marking of the lamina cribrosa, etc. (30 diameters).

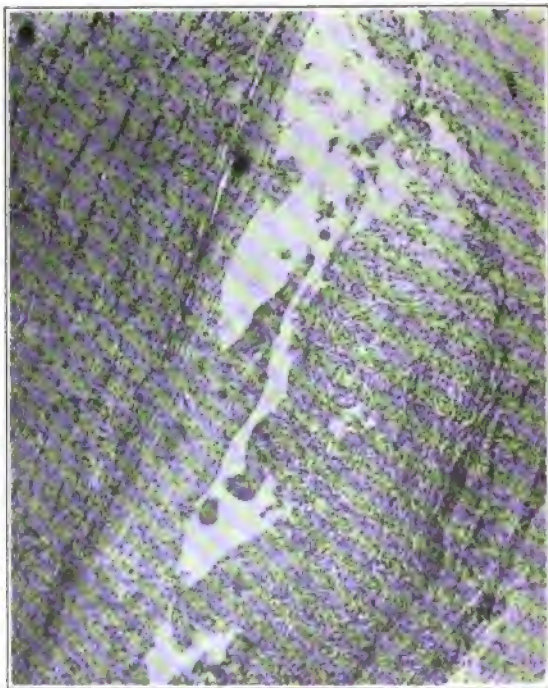


FIG. 10.—Showing the ampullated portion of the vaginal sheath largely obliterated by the formation of new tissue (40 diameters).



tissue elements and infiltration with lymphoid cells. In many of the vessels hyaline thrombi can be seen (Fig. 7). These alterations are also present in the vessels of the papilla (Fig. 8). The nerve fiber layer is about double its normal thickness, and gives clear evidence of marked œdema.

*Optic Nerve.* The papilla is swollen and extends well above the retina. The physiological cup is filled with new connective tissue (Fig. 9), which passes across the surface of the papilla and extends to the retina immediately adjacent. This new tissue shows only slight metamorphosis, the cellular elements still being abundant. The nerve fibers are tortuous and separated; in many of the interstices between them serous and fibrinous exudates can be made out, although, as a rule, the spaces are clear. Throughout the papilla can be seen thrombosed capillaries and hemorrhages both large and small. In places the hemorrhages have broken through and appear on the surface of the disk. The transverse markings of the lamina cribrosa are lost. The body of the nerve is swollen, the nerve bundles are separated, and there is some lymphoid infiltration and neuroglial proliferation. The dural sheath is much thickened. The ampulla is distended and filled with new tissue (Fig. 10). There is a fairly widespread distribution of hematogeneous pigment throughout the nerve head.

*Choroid.* There is every evidence of congestion with œdema. Many of the vessels are greatly distended and others show endothelial proliferation. There is no evidence of inflammatory reaction.

**COMMENT.** The nature of the cerebral lesion in nephritis, which is responsible for the symptom-complex of uremia, has long been a subject of conjecture; and conjecture in regard to pathological processes breeds disagreement. The view most widely accepted attributes the symptoms to some toxic disturbance arising either in a disordered metabolism or in the retention of some products of normal metabolism which fail of elimination through the diseased renal epithelium.<sup>2</sup> A similar disagreement exists in regard to the agency which produces in nephritis the well-recognized alterations in the eye-grounds, they being more commonly attributed, as the term albuminuric neuroretinitis would indicate, also to a disturbance—an inflammation in this case—of toxic origin.

In addition to the objective changes visible with the ophthalmoscope, there often occur in chronic renal disease, even in the absence of a state justifying the term uremia, a number of subjective symptoms directly comparable to those seen in conditions known to be associated with an increase of intracranial tension—more particularly

<sup>2</sup> On the toxic theory, it has always been difficult to explain the absence of uremic symptoms in cases of complete suppression of urine in which a large excess of urea and other excrementitious products occurs in the blood.

headache, nausea or vomiting, drowsiness, and vertigo—not to mention the rhythmicities of pulse and respiration, often of a Cheyne-Stokes type, which may be present in the later stages.<sup>3</sup> In consequence of this, the differentiation between nephritis with cerebral symptoms and an intracranial abscess, tumor, hemorrhage or serous meningitis co-existent with albuminuria, often presents great difficulties; and this is the more so since in the former condition definite focal symptoms, such as aphasia, temporary amaurosis (independent of the changes in the fundus oculi), hemiplegia, localized paralyses, Jacksonian epilepsy, and the like, may arise.<sup>4</sup>

It seems to have been first suggested by Traube (1861) that these symptoms in nephritis, so characteristic of an increase of cerebral tension, might actually be due to a cerebral oedema—a mechanical process, therefore—rather than to any autotoxic disturbance; this abandoned hypothesis has of late years been seriously reconsidered by Byrom Bramwell, A. E. Russell,<sup>5</sup> and others. Local oedemas, furthermore, most easily account for the focal palsies of cerebral origin which not infrequently occur in cases of advanced renal disease—palsies which remain unexplained in the absence of any lesion demonstrable after death. Doubtless for the reason that oedema is an evanescent condition, effectually masked by the usual methods of hardening tissues, these views in regard to the causation of symptoms have been the outcome of clinical and experimental studies rather than of postmortem examination of the tissues concerned.

Any swelling of the brain, be it a general or a circumscribed process, necessarily leads to compression symptoms, the eye-grounds furnishing at an early stage an objective and sensitive index of the process. This is even more true of oedema than of states of increased cerebral pressure due to an encroachment on the intracranial space by a solid growth or an abscess.

Thus neuroretinal changes characterize a number of conditions associated with cerebral oedema—notably they are seen after cranial traumatism which has led to cerebral contusion; after thrombosis or embolism in which the area of softening swells from inhibition of fluid; they also accompany the "wet brain" in acute alcoholism and the so-called serous meningitis of febrile and other states; they are not uncommonly seen in cases of cerebral arteriosclerosis. Indeed, in many cases of tumor, areas of oedema due to circulatory disturbances may occur in parts remote from the growth, giving false

<sup>3</sup> The high pressure pulse in these cases of renal disease with cerebral symptoms need not of course be primarily attributable to the acute increase of intracranial pressure, although some have attempted to associate the conditions. In this patient under discussion, for example, the decompression had only a transient and slight effect in lowering the high blood-pressure; whereas, for comparison, in cases of intracranial tension due to hemorrhage an immediate and permanent fall in pressure occurs after a successful decompression.

<sup>4</sup> Riesman: Uremic Aphasia, *Jour. Amer. Med. Assoc.*, October 11, 1902, p. 883.

<sup>5</sup> The Pathology of Uremia, *West London Med. Jour.*, January, 1907.

localizing signs (Collier); and it is presumable that, in the absence of tumor, local œdemas from one cause or another may sometimes occur which so closely simulate the picture of a rapidly enlarging growth as to make the processes clinically indistinguishable—the so-called “pseudotumor” of Nonne<sup>6</sup> comprising a group of supposed tumor cases in which there has been either a spontaneous recovery or in which the symptoms have been permanently relieved by decompression or, in case of death without operation, in which no lesion whatever has been disclosed at autopsy.

The swelling of the brain from œdema, particularly after traumatism and in serous meningitis, is associated with an excess of fluid under increased tension in the cerebrospinal spaces, and in favorable cases a lumbar puncture, or repeated punctures, may suffice to tide over the period of pronounced compression symptoms. Seemingly the same condition exists in uremia, and of late years, since attention has been drawn to this matter, there have been a number of recorded instances in which uremic coma and convulsions have been markedly relieved after the withdrawal of fluid by a lumbar puncture.<sup>7</sup>

We have been given the privilege in Dr. Barker's service during the past two or three years of observing a number of patients with renal disease, suffering from headache and vomiting, in whom the usual so-called albuminuric retinitis was present. In a number of instances a continuous examination of the eye-grounds has been made coincident with the withdrawal of the subarachnoid fluid from the lumbar region. Striking changes, particularly in the vascular condition—chiefly shown as a straightening of the veins and narrowing of their caliber—have been demonstrable under these circumstances, and, not uncommonly, for the time being there has been a distinct lessening of the headache and nausea. In a number of cases, particularly when the process has not been of long standing, a measurable subsidence of the swelling has promptly occurred. These changes, as might be expected, are usually transient, and in the course of a few hours, or, in exceptional cases, of a few days, with the re-accumulation of fluid it is usual for the preëxisting condition to become reëstablished.<sup>8</sup>

<sup>6</sup> Fälle von Symptomenkomplex “Tumor cerebri.” (Pseudotumor cerebri.) *Deut. Zeit. f. Nervenheilk.*, 1904, vol. xxvii, p. 169; also *Neurolog. Centralbl.*, 1905, vol. xxiv, p. 1077. Cf. also H. H. Hoppe: Brain Tumor Symptom Complex with Termination in Recovery. *Jour. of Nerv. and Ment. Dis.*, February, 1907.

<sup>7</sup> Purves Stewart: Significance of the Cerebrospinal Fluid. *Edinburgh Med. Jour.*, May, 1906, p. 439. Also A. E. Russell: The Pathology of Uremia. *West London Med. Jour.*, January, 1907; Scherb: *Revue Neurologique*, vol. x, No. 1, p. 19, Willson: *Jour. of the Amer. Med. Assoc.*, 1904, etc.

<sup>8</sup> When the swelling of the disk and retina is due to edema alone, in the absence of the infiltration which occurs in consequence of stasis of long standing, the subsidence of the swelling may be very rapid. In experimentally induced choked disk, brought about by allowing fluid to enter the subdural space under tension, the swelling may appear after a few minutes of compression, and will as rapidly subside when the pressure has been withdrawn.

Similar observations, in accord with those of others, have been made by us on a few cases of eclampsia in Dr. Williams' service. In one of these patients in whom the symptoms had been acutely acquired, a prompt subsidence of the choked disk ("neuro-retinitis") occurred after the puncture, with early disappearance of all of the so-called albuminuric changes, except the hemorrhages, which slowly absorbed. In this connection Slemmons' studies<sup>9</sup> on "eclampsia without convulsions" are interesting, and go to show that symptoms of cerebral pressure of a degree not sufficient to cause convulsions may coincide with albuminuria in pregnancy, and may even be fatal, with a postmortem disclosure of the characteristic lesions of eclampsia. Slemmons concludes that the clinical observations which he has made strongly indicate a high tension within the cranium. Unfortunately in his cases no ophthalmoscopic examinations were made.

With these observations in mind, and in the light of our favorable experience with decompression for the cerebral oedema following fractures of the cranial base, we were led to suggest decompression in the patient whose case has been recorded, on the assumption that the uremic symptoms were attributable to cerebral oedema, and the changes in the eye-grounds, at least in part, to the cerebrospinal fluid stasis in the optic sheath produced by this same intracranial disturbance. The outlook for the patient, as less radical measures had failed, was most forlorn, and the attempt had its justification in the subsequent marked improvement which enabled her to leave the hospital in a few weeks, at least subjectively well.

So far as we are aware this is the first case of a deliberate surgical intervention in a case of uremia on the view of its being a pressure phenomenon. It, however, is not the first recorded case of operation. In his *Clinical Studies*, Byrom Bramwell<sup>10</sup> relates the history of a patient who, some years ago (1893), was admitted to the Edinburgh Royal Infirmary, suffering from headache, vomiting, optic neuritis, giddiness, and convulsions—symptoms which had arisen during the course of a recent pregnancy. A differential diagnosis lay between cerebral tumor, cerebral abscess, and uremia, and inasmuch as the symptoms presented certain unilateral features and an examination disclosed a discharging otitis media, the preferential diagnosis was cerebral abscess. An operation by Mr. Cotterill, exposing the left temperosphenoidal lobe, showed an increase of pressure, but failed to disclose an abscess. One of three exploratory punctures was followed by the evacuation of an abundance of cerebrospinal fluid, evidently from the ventricle. "The patient made an uninterrupted recovery, the headache and vomiting speedily subsided, there was no return of the epileptiform attacks, the optic

<sup>9</sup> Eclampsia Without Convulsions. Johns Hopkins Hospital Bulletin, 1907, xviii, p. 448.

<sup>10</sup> Clinical Lecture on Uremia and its Treatment. *Clinical Studies*, 1906, N. S., v, p. 1.

neuritis immediately declined, and in the course of a few days entirely disappeared." Bramwell goes on to say that this case and its remarkable improvement suggests the advisability of trephining for the relief of increased intracranial pressure in such cases of uremia as have failed to be relieved by the ordinary remedies.

Experiences of this kind naturally serve to support Traube's hypothesis that the symptoms of uremia are produced by cerebral oedema, although Traube's explanation of the process—namely, that increased arterial pressure due to hydremic plethora and hypertrophy of the left ventricle, is the cause of the oedema, this, in turn, leading to vascular anemia through pressure—will perhaps not be accepted by all.<sup>11</sup> Gowers,<sup>12</sup> for example, pointed out that, although the cardiac hypertrophy and the retinal lesion commonly correspond in the time of their appearance, the latter is, nevertheless, occasionally found in the absence of the former.

The difficulty at times of distinguishing between cases of brain tumor or abscess and cases of nephritis with cerebral symptoms must have been experienced by many. A number of illustrations of this have come under our observation—of patients who have been admitted to the surgical wards with a diagnosis of neoplasm, extensive renal disease having subsequently been found; and, on the other hand, of patients who have died after a prolonged treatment for nephritis, in whom autopsy has disclosed an intracranial growth. It may be added furthermore that we have frequently seen in tumor cases an ophthalmoscopic picture the counterpart of what is supposed to characterize the retinal changes of nephritis, and, vice versa, the typical picture of the choked disk of tumor in cases of nephritis.

It must be granted that the symptoms characterizing uremia, and what interests us even more, the alterations of the eye-grounds in nephritis, can be attributed in part, if not wholly, to the mechanical effects of increased intracranial pressure resulting from cerebral oedema. It is a quibble to refer the oedema back to some toxic agency. In a sense, of course, all oedemas are remotely due to toxic disturbances; for example, the swelling of an extremity (*Stauungs-hyperämie*) which results from the application of a tourniquet is really toxic, although the oedema has been primarily brought about by a mechanical agency. The discomfort of the swollen foot in the tight boot would be lessened under these circumstances by slicing the leather, just as are the discomforts of the tense brain by opening the dura. In regard to uremia, therefore, to be conservative, we may at least say that the symptoms are elicited by oedema resulting from some toxic agency, and are not, as is commonly supposed, due to the direct effect on the cerebral tissues of the toxic agent alone.

We believe, from our clinical and experimental studies of choked disk, that the oedema of the retina itself is due in large part, even in

<sup>11</sup> Senator's discussion in Nothnagel's System, "Diseases of the Kidneys," American edition, 1905, p. 102.

<sup>12</sup> Medical Ophthalmoscopy, 1890, 3d ed., p., 213.

these cases of nephritis, to a backing of cerebrospinal fluid under increased tension into the investing meningeal sheath of the optic nerve. In this patient's case the rapid and pronounced subsidence of the swelling, in spite of its long duration, of its unusually high grade, and of the accompanying round-cell infiltration and organization which we were able to demonstrate histologically, would seem to add further confirmation to this view.

Although the chief reason for presenting this individual history was the opportunity of discussing the matter already alluded to, there are some other points which may deserve mention—among them, the terminal event in this unfortunate girl's life. As cited by Byrom Bramwell, it is Rose Bradford's view that uremia occurs more frequently in the young and as a symptom of the "small white" rather than of the "small red granular" kidney. In his Goulstonian lectures<sup>12</sup> he says: "In the great majority of cases of acute uremia in which coma is developed the insensibility is preceded by a convulsive seizure or series of epileptiform attacks. But cases are occasionally met with in which sudden coma due to uremia occurs without any preceding convulsion. These cases are very rare and are apt to give rise to great difficulty in diagnosis, for suddenly or rapidly developed coma occurring in the course of disease of the kidney . . . is highly suggestive of cerebral hemorrhage—much more suggestive of cerebral hemorrhage than of uremia." Comment has already been made, in the relation of the patient's history, upon the failure clinically to recognize the fact that she had suffered from an apoplectic stroke, the difficulties of this perhaps having been enhanced by the comparatively slow march of her symptoms owing to the cerebral protrusion which was made possible by the former decompression operation—a protrusion which obviated the acute pressure symptoms which under other circumstances would, in all probability, have been more promptly fatal.

*Conclusion.* In view of the marked improvement after cerebral decompression, this case adds further evidence in support of Traube's hypothesis (favored by Bramwell, Russell, and others) that the cerebral symptoms present in the so-called state of uremia are largely due to pressure from oedema of the cerebral tissue.

It goes to show, furthermore, that the condition of so-called albuminuric neuroretinitis is, in large part at least, a local oedema of mechanical origin.

The case suggests the propriety of permanent decompression in selected instances of renal disease when medical measures or lumbar puncture have failed to relieve existing cerebral (uremic) symptoms, or when blindness is threatened owing to rapidly advancing degenerative changes of the neuroretinal tissues.

<sup>12</sup> Rose Bradford: Observations on the Pathology of the Kidneys. *The Lancet*, April 2, 1898, p. 916.

**PHYSICAL THERAPEUTICS.<sup>1</sup>****By R. TAIT McKENZIE, M.D.,****PROFESSOR OF PHYSICAL EDUCATION IN THE UNIVERSITY OF PENNSYLVANIA,  
PHILADELPHIA.**

EXERCISE as a therapeutic agent must include all means by which the body may be acted upon by movements, active or passive, performed by means of the patient himself, the hand of an operator, or a machine devised for that purpose.

**ACTIVE.** By making the definition comprehensive, we bring in all the more active forms of exercise, such as games, in which the modern man strives to preserve and cultivate these old coördinations of throwing, catching, striking, climbing, leaping, and running, that instinct has told him are necessary for self-preservation and complete symmetrical development. The popularity of such games as golf is an example of the way in which the cry of the muscular system for exercise is answered by the sedentary office worker. It is, however, the accurate and direct therapeutic application of exercise in its many forms that must be considered in this discussion.

(a) *Effort.* Active exercise may be divided into "exercises of effort" and exercises of "endurance." In exercises of effort, muscular contraction is violent and the attention concentrated on one or two contractions only. The breath is usually held and the blood pressure rises enormously and suddenly, going down again rapidly to normal, more quickly than the pulse rate. Weight lifting, throwing, jumping, and vaulting are examples. The danger in these exercises lies in muscular overstrain, hernia, or in the rupture of sclerosed arteries, or overdilatation of a defective heart.

(b) *Endurance.* In exercises of "endurance" easy movements are repeated until the onset of fatigue. In such exercises the blood pressure rises more slowly and remains high, even after the pulse rate has gone down. Walking is perhaps the best example. In a toxic dose we get fatigue "fever," the temperature going up to 102°, and restlessness, insomnia, albuminuria, seminal emissions, and general muscular stiffness and soreness, lasting several days.

Many exercises combine both, like boat-racing or middle distance running, in which there are a series of maximum efforts lasting up to twenty minutes with no intervals of rest. The tax is here on the circulatory apparatus, and in such men we would look for heart dilatations and hypertrophy. The most careful investigation shows, however, that the healthy heart is not so effected, permanently, at least, and that the remote after-effects are practically negligible. The history of 'Varsity crew men, as shown by the investigations of

<sup>1</sup> Read at a meeting of the Association of American Physicians, Washington, D.C., May 12 and 13, 1908.

Morgan, in England, and Meylan, in America, shows an expectation of life of two to four years above the selected lives of the actuarial tables of life insurance companies. Roughly speaking, exercises of "effort" are more suitable in youth, while exercises of "endurance" are better borne by those of more mature years.

(c) *Duplicate Movements.* In duplicate movements the direction of the movement is controlled, and the amount of resistance applied by the hand of the operator is estimated and prescribed. In therapeutic language, the dose is measured. In the Zander method of mechanotherapy the hand is replaced by the weighted lever of a machine, acting so that the heaviest pull comes on the muscle when in its best position for action. The advantages of such movements are: (1) The accuracy of the movement; (2) the power of isolating the groups of muscles involved; and (3) their capacity for stretching contracted parts.

**PASSIVE.** In passive movements the patient's will-power is not exerted, and the circulation in the muscle itself is improved mechanically, much as respiration is re-awakened in the drowned man by the expansion and contraction of the chest walls.

*Massage.* Passive exercise is given in the form of massage in its various manipulations of stroking, kneading, pinching, striking, or shaking, or by machines like the "tower," the "camel," and the "horse" of Zander, or by the innumerable vibrating machines that are the rank growth from the seed planted by him thirty years ago.

There is such wide divergence of effect from different forms of exercise that the nature and amount of movement to be applied in a particular case may be attended with considerable difficulty and risk, accuracy being the most important factor in outlining a course of treatment. Even in the universal exercise of walking, the change of pace from three to four miles an hour changes a listless amble into a vigorous exercise, and mountain climbing is, after all, just walking up a slope, while the fatigue of walking over broken ground or along a rail, where the attention must be kept on the track, involves close mental concentration, in what would be an entirely automatic exercise on a level road.

*Posture.* The most obvious application of exercise is to the many faults of posture that result in deformity to the yielding structures of the spine and arch of the foot. The exaggeration of the normal anteroposterior physiological spinal curves to the pathological condition, known as "stooped shoulders" or "round back," or to the various lateral deviations, with rotation of the vertebræ, grouped under the name of scoliosis, are examples; over 90 per cent. of such cases are due to some form of muscle fatigue.

To offset the freedom due to the upright position, we must consider the disadvantages of support by one pair of limbs, the other acting as weights to be carried, a disadvantage that is intensified



during the growing period by long hours of comparative stillness, in which these forces can act unimpeded. The success of the treatment in these cases must rest on exercises applied, first, to reëducate the patient in the correct position of standing, sitting, and lying; and in more severe cases, to stretch contracted ligaments shortened by habitual malposition. Any mechanical support must be looked upon only as a means to retain the improvement gained by these active means.

The isolation of muscular action is particularly important in a delicate patient with but small constitutional reserve, who would soon suffer general exhaustion from loosely prescribed inaccurate movements involving many and large groups of muscles that do not directly bear on the condition to be treated.

*Flat Foot.* In flat foot the reëducation of the muscles that act with the ligaments in supporting the plantar arch is a most valuable auxiliary to the usual treatment by support, and in some cases may in itself be sufficient to produce a cure.

*The Heart.* An entirely different application of exercise is that to diseases of the heart and circulation, and we owe to Oertel, of Munich, the first demonstration of its possibilities in this direction. Himself an invalid at thirty, with a fatty dilated heart and œdematous legs, he had to give up practice completely. He improved his own condition by a system of graduated walks of increasing length and up increasingly steep slopes, accompanied by limitation of fluids and a restricted diet, until his œdema, palpitation, and other symptoms of distress had completely disappeared by this muscular training and drying-out process, and he was able to resume his practice, which he carried on actively for over twenty years. He established his cure at Reichenhall, where the mountainous paths about the village were lined by rest benches and marked by colored bands attached to the trees distinguishing the slope and distance. By these means the amount and severity of the exercise could be prescribed with accuracy to his patients.

This method has been largely superseded, or rather preceded, by the more gentle and more widely applicable treatment introduced by the Schott brothers, Theodore and Auguste, and practised widely both in Europe and America. Exercise is here used in combination with carbonated brine baths. The technique of the baths I need not enter into here, but the exercises are simple and efficient in reducing the rate and increasing the volume of the pulse, and in materially reducing the area of heart dulness. They consist of a series of nineteen duplicate movements of the simplest character, each done slowly and once only, with long rests between. They begin with five for the arms, three for the trunk, four for the arms, four for the legs, one for both arms, and two for the hand and foot, the whole treatment lasting about twenty minutes. They may be given even when compensation is not established, and some of them may be given to a

bedridden patient. The effect is a slowing and strengthening of the pulse and a reduction of the dilatation, lasting for several hours and accompanied by great relief of the most distressing symptoms of dyspnoea and palpitation.

The conditions that lend themselves especially to this treatment are dilatation from fatty deposits about or in the substance of the heart muscle, and valvular insufficiency. The contra-indications are arteriosclerosis and profound anemia.

*Obesity.* Obesity is a condition that can be controlled often by exercise alone, whether the heart muscle is normal or not, but care must always be exercised in the selection of cases. The best results are obtained in patients up to thirty-five or forty, who are anxious to reduce their weight, whose hearts are sound, and whose deposits of fat are localized in the pericardium, omentum, and mesentery. In those of advancing age, and when the obesity is extreme and the vital energies are beginning to fail, a reduction course would accelerate decay and lead to rapid loss of strength and functional power, with the continual risk of heart strain, arthritis, and renal disease. A course of treatment should include regulation of diet, limitation of fluids, and the application of daily exercise of increasing severity for a period of about five weeks, followed by a period of one week's rest to watch the daily variation of weight. If necessary, the course should be repeated from time to time. The exercises should begin with trunk flexions, extensions, and rotations taken recumbent at first, followed by thigh flexions, extensions, adductions, and abductions, introducing, as they do, the action of large muscle masses. As the muscular tone improves, walking and hill climbing can be begun cautiously, as in the Oertel cure, and increased according to the strength and willingness of the patient. When this course is combined with the limitation of fluids, starches, and sugars, and the exhibition of thyroid extract, the results are sure and the reduction can usually be maintained with but little effort.

*Constipation.* Constipation is so frequently the direct result of sedentary habits that exercise at once suggests itself as a valuable means of controlling this disorder, and it is applied successfully in many forms. Horseback riding or the saddle-backed machine of Zander, known as the camel and the horse, are means of agitating the abdominal contents and stimulating the peristalsis. All movements of flexion and rotation of the trunk on the pelvis produce a massage of the abdominal contents, and the contraction of the abdominal muscles acts on the contained viscera, stimulating the portal circulation and causing contraction of the intestinal walls, while by the deep kneading of massage the course of the colon may be followed and the contents mechanically pushed forward. A less efficient substitute for the trained human hand is found in the Zander machine, in which balls rotate on an arm and follow the general course of the colon in a circular direction. A treatment of twenty minutes,

beginning with free stretching movements, going on to trunk flexions, and ending with slow deep massage, following the course of the colon, is the most effective way in which exercise may be applied to this condition and improvement should appear from the first.

*Hernia.* In many cases, the general relaxation of the abdomen shows itself in dilated abdominal rings and the presence of, or tendency to, inguinal hernia. A hernia that is supported almost always shows an inclination to recovery, and this can be greatly hastened by the development of the abdominal muscles, which strengthen and keep both abdominal rings intact. The development of the internal oblique in its lower fibers, strengthening the internal ring, for which it forms a lid, and of the external oblique, whose pillars narrow the external ring, would be indicated. When complete hernia is actually present the greatest care must be exercised to protect the abdominal rings while the exercises are being performed and in the intervals. This may be done by training the patient to use the second finger like the pad of a truss during a treatment.

*NERVOUS SYSTEM.* The therapeutic effect of massage, mechanical vibration, and exercise on diseases of the nervous system is obtained through their power to control pain, to improve local nutrition, to prevent or stretch contractures, and to educate and train coördinations that are either undeveloped or have been partly lost.

*Neuralgia.* In neuralgia massage is frequently of the greatest service in improving the circulation and elevating the temperature of the part, while the relief afforded by friction and kneading of the whole scalp in headaches is well known.

*Neurasthenia.* In the Weir Mitchell cure for neurasthenia exercise plays an important role during convalescence, beginning with massage to make the assimilation of food more complete, and ending with more and more active exercise, according to the patient's condition.

*Paralysis.* In preserving the nutrition of the muscles in infantile paralysis, massage is of the greatest value. It is, with heat, our main resource, and in the reestablishment of control and the reëducation of the damaged nerve centres its value is incontestable. The voluntary action of the affected muscles may be fostered by exercises in which the will-power of the patient is employed and concentration of the attention is trained.

*Stammering.* It is through the motor tracts that disorders of coördination are to be reached. The treatment of stammering by the reëducation of the breathing mechanism and that of phonation, as practised by Hudson Makuen, is a case in point. The two coördinations are taken separately and then combined in such a way as to get the complete and coördinate sound, a combination that is not lost when once established on this firm physiological basis.

*Tabes Dorsalis.* The symptom of ataxia in tabes dorsalis has been successfully treated for many years in Germany, Sweden, and

America, but the most complete and exhaustive description of it is that by Fränkel, of Heiden, in his book on the subject. In these patients the relaxation of the ligaments is accompanied by over-extension of the joints, flabbiness of the muscles, but no apparent loss of muscular power. The symptom against which the exercise treatment is directed is the motor disturbance which has its origin not in the diminution of the motor function of the muscles, but in a loss of sensibility. Improvement is brought about through the capacity of the nervous matter to be exercised so long as the motor apparatus itself is intact.

It is a re-acquisition of ordinary movements lost in consequence of partial or total loss of sensibility, a principle identical with the acquisition by a healthy person of a more complicated coördination, such as juggling or balancing. Patients who are equipped from the start with what may be called the muscular sense or intelligence will, in consequence, make more rapid progress than those who have never had this equipment. Personal courage is an important factor, persistence, and the determination to succeed. At the beginning the simplest coördination must be re-taught, the rising from a chair, sitting down, walking, mounting and descending a stairway, etc.

Exercises are taken lying down, sitting, standing, walking forward, backward, and zigzag. Continuous movements, like following a line with the hand or foot, the accurate pointing to a peg or hole by foot or hand, are taught by various ingenious devices that teach the patient to keep the arm or leg raised in a certain position, and from that position to make excursions in which two or more joints are involved in movements whose course varies at every movement.

The precautions to be observed depend on the loss of sensibility, which means that the sense of fatigue is not felt, and exhaustion even after a slight amount of work becomes extreme, as shown by the rapid increase of pulse rate without the characteristic feeling of tiredness. The necessity of concentrating the attention, the muscular exertion, the fear of accidents, the annoyance of failure, all produce rapid fatigue, so that a treatment must last not over three or four minutes, with pauses between movements, to allow of complete recovery. The improvement in the ataxia is unfailing, and although the ideal result, a restoration of the normal accuracy, character, and velocity of the movements, is not often attained, the restoration of the powers of locomotion and coördination are usually sufficient to enable the patient to resume his business or profession, while the scientific interest centres in the phenomenon of the improvement of a symptom, which is the result of an organic lesion.

It will be seen, then, that exercise in its application to pathological conditions of posture, of nutrition, of the circulation, and of the nervous system must depend for its success upon careful selection and accuracy of the kind of dose employed, and on persistence in following out a course of treatment. It is the neglect of these con-

siderations that is responsible for most of the failures in its application.

So often exercise occupies the borderland between education and therapeutics that it is not surprising if the lay educationalist is sometimes tempted on to the unknown land of the pathologist, to the discomfiture of his theories, and the physician too often fails to appreciate the range and effectiveness of this most powerful and versatile system of therapeutics which is always his to command.

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## THE PRESENT STATUS OF SERUM AND VACCINE THERAPY.<sup>1</sup>

BY MARK WYMAN RICHARDSON, M.D.,

OF BOSTON.

IN the early nineties the study of the poisons of diphtheria and tetanus, and the successful production, through animal inoculation, of specific antidotes for those poisons, led not unnaturally to the hope, if not to the actual expectation, that a great principle had been discovered which should apply equally well to all bacterial disease. More than a decade has passed, however, and, speaking broadly, the great mass of bacterial disease remains outside the antitoxin category, and speculation has had to seek other theories to explain the immunity acquired after infection with organisms, such as typhoid and allied bacilli, the cholera spirillum and the various cocci.

Experiment soon showed that, in the fight against this class of organisms, nature directed her efforts, for the most part, against the bacteria themselves, and not, to any marked extent, against their toxins. An immense and valuable literature grew up covering the bactericidal and bacteriolytic sera (Pfeiffer). Strenuously opposed to this—the “humoral” school of the Germans—was the phagocytic school of the French, led by Metchnikoff. Each party claimed exclusive possession of the truth, but, as is commonly the case, time has shown that both have their proper spheres of influence, and, more recently, extracellular bacteriolysis has had to yield important ground to the specific opsonin and phagocytosis. Bacterial destruction, however whether it be by bacteriolysis or phagocytosis, is not without its disadvantages; it may be, in fact, a sort of double-edged sword, for disintegration of the invading organisms sets free their poisonous contents, and disastrous intoxication may be the result.

Until very recently there has been a sharp distinction drawn between these intracellular or endotoxins, seen in typhoid fever, cholera,

<sup>1</sup> Read at a meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1908.

dysentery, etc., and the extracellular toxins of diphtheria and tetanus. The bacilli of diphtheria and tetanus produced as a result of growth in a fluid medium a soluble toxin, which, when inoculated into a proper animal, caused the formation of a specific antitoxin, and this antitoxin united with and rendered inert definite amounts of toxin. The organisms of the second group, however, produced practically no toxin in fluid media. If disintegrated in any way, as by trituration when dry or frozen (liquid air), or by autolysis, they gave up their endotoxin. To this endotoxin, in animal experiments, could be produced a certain amount of toleration, but antitoxin production in any proper sense (obedience to the law of multiples) was not observed.

Here again, however, clear-cut, diametrically opposed ideas have had to yield, and we now have good evidence that organisms, such as typhoid, dysentery, or plague, *can* produce soluble poisons, and that antitoxins of a moderate strength can be obtained.

In this connection it is interesting to note, too, that other possible means for rendering bacterial poisons innocuous are being suggested. Flexner, for instance, has pointed out the possibility that, in the process of opsonification and phagocytosis, the bacterial endotoxins might be broken up into less harmful compounds, and a condition of detoxication thereby brought about. Emmerich and Loewe, too, claim for their pyocyaneus enzymes the power, not only to kill diphtheria bacilli, but to neutralize their toxins.

Although the chief studies in immunity have had to do with bacteria and the infections produced by them, this field of research has been broadened very markedly in recent years, so that a great variety of animal and vegetable cells and poisons, with their corresponding antibodies, have been the subject of extensive investigation. Thus, we have hay fever antisera specific for certain vegetable pollens, antitoxins for snake venoms, and antisera for nearly every variety of animal cell, most important of which are the antitoxic and cytotoxic sera for hyperthyroidism.

Most of these antisera have been produced by inoculation of specific substances into the lower animals. The blood serum of these animals, when transferred to other animals and to man, have given varying degrees of passive immunity.

More recently the attempt has been made to do away with the animal inoculation, and by the direct incorporation of morbid material to protect actively the human individual against special disease, or if already sick to hasten his cure. This method of treatment with specific vaccines is one of very wide application and of great promise. Finally, the observed natural antagonism of one disease process for another has led empirically to the artificial induction of the one for the cure of the other. This antagonism is made use of in the treatment of sarcoma and leukemia by the toxins of streptococcus and bacillus prodigiosus (Coley). In the same

category would be placed the treatment of diphtheria by the filtrates of pyocyanus cultures—pyocyanase (Emmerich and Loewe).

**NORMAL SERUM.** Before taking up the question of specific immune sera in therapeutics, it will be well perhaps to consider briefly the uses to which simple normal blood serum has been put. Most important in studies upon bacteriolysis and hemolysis, as furnishing the digestive ferment or complement essential for the completion of those processes, fresh normal serum has not fulfilled the hopes once entertained for it as a therapeutic agent in bacterial disease, either alone or combined with specific antisera.

The most important use of fresh normal serum is seen, perhaps, in the prevention and cure of hemorrhage. This subject has been studied especially by Weil,<sup>2</sup> who finds that fresh blood serum is markedly efficacious in the prevention and cure of hemorrhagic dyscrasias associated with defective coagulation power. Much benefit has been seen in hemophilia, be it of the spontaneous or inherited type, in acute primary or secondary purpura with hematuria or hemarthrosis, or in severe anemias with a tendency to hemorrhage.

As a prophylactic measure when unavoidable operations are to be performed upon hemophiliacs, or when, as in jaundice, uncontrollable hemorrhage may be expected, the exhibition of fresh serum is of great service. It is given either intravenously or subcutaneously in doses of 15 to 30 c.c., and takes effect in twelve to twenty-four hours. Improved conditions persist one to three months. Human serum is most effective, but horse and rabbit sera are good. In default of other sera fresh diphtheria antitoxin can be used. Aside from its general use, local applications of serum to bleeding points or surfaces are said to exert marked styptic power.

Because, in animal experiment, injection of sterilized horse serum into the peritoneal cavity caused a marked determination of leukocytes toward the point of injection, with resulting increased resistance to infection with *Bacillus coli* and *Staphylococcus pyogenes*, Petit<sup>3</sup> has used this serum as a local application in more than 100 cases of human infection. Non-septic abdomens have been washed out with the serum to make them more resistant to possible infection, and already septic abdomens, septic uteri, and septic open wounds have been packed with gauze saturated with the serum with excellent results as to healing and cicatrization.

**ACTINOMYCOSIS.** Wynn<sup>4</sup> has treated a case of actinomycosis of the lung with a specific autogenous vaccine. A forty-eight-hour agar culture was heated to 60° C. for one hour. It was then ground up in an agate mortar and suspended in normal salt solution with 10 per cent. of glycerin; 1 c.c. of this suspension was equal to 1 mg. of "actinomycin." Beginning with a dose of  $\frac{1}{1000}$  mg., six inocu-

<sup>3</sup> International Clinics, Seventeenth Series, vol. iv.

<sup>4</sup> New York Med. Jour., June 22, 1907.

<sup>4</sup> Brit. Med. Jour., March 7, 1908.

lations were made in eleven weeks. General and local improvement was rapid, and patient was well one year after last inoculation.

**ANTHRAX.** Legge<sup>5</sup> collected 65 cases of anthrax with 2 deaths under treatment with a specific antiserum prepared according to Sclavo. The serum is produced by inoculation of asses first with bacterial vaccines, then with living cultures of increasing virulence. The serum is thought to be not especially antitoxic or bactericidal, but to act by stimulation of phagocytosis. The dose is 40 c.c. and is given subcutaneously. Marked improvement is seen in the patient's condition by the third day.

**CANCER.** Paine and Morgan<sup>6</sup> subjected Doyen's anticancer serum to critical tests, and found it entirely lacking in power, clinically and experimentally. *Micrococcus neoformans*, the cause of cancer, according to Doyen, and by the inoculation of which the anticancer serum was produced, was found by Paine and Morgan only rarely in malignant tumors, and then most presumably through some contamination. In animal experiment this organism produced no tumor formation; moreover, Doyen's own experimental tumors represented only inflammatory tissue.

**CEREBROSPINAL MENINGITIS.** In no disease has serum treatment made more advance in recent years than in cerebrospinal meningitis. Most important in this advance has been the work of Flexner<sup>7</sup> and his associates. Briefly, the serum is produced in horses by subcutaneous inoculation of dead cultures, living cultures, and autolysates of dead cultures. Many different strains of the meningococcus are used. After a year of immunization the serum of such a horse has been used intradurally after lumbar puncture in 130 cases, with 35 deaths, a mortality of 27 per cent. The dose is 20 to 30 c.c., and may be repeated daily for four to five days if necessary. When cases are treated within the first twenty-four hours the results are most brilliant.<sup>8</sup> The serum seems to act by stimulating phagocytosis, which destroys cocci and renders harmless their endotoxins.

Quite similar results have been seen in Germany. For instance, Levy,<sup>9</sup> using a serum prepared by Wassermann, had a death rate of only 11.76 per cent. in 17 cases in which the serum was given intradurally. In 14 untreated cases the mortality was 78 per cent. Very interesting is a case of cerebrospinal meningitis described by Peabody.<sup>10</sup> The infecting organism was, in this case, the streptococcus. Six intradural inoculations of streptococcus serum in doses of 10 c.c. each were given in eight days. After the second inoculation the spinal fluid became sterile and remained so. Clinically, the patient improved rapidly and recovered.

<sup>5</sup> Brit. Med. Jour., 1905, vol. i.

<sup>6</sup> Med. Chir. Trans., London, 1906, 707.

<sup>7</sup> Flexner and Jobling. Jour. Exper. Med., 1908, No. 1.

<sup>8</sup> Dunn. Boston Med. and Surg. Jour., March 19, 1908.

<sup>9</sup> Deut. med. Woch., January 23, 1908.

<sup>10</sup> Med. Record, March 14, 1908.



This success with a streptococcic meningitis suggests immediately, of course, the treatment of other bacterial invasions of the meninges (pneumococcus or typhoid bacillus) with corresponding antisera. It is more than probable that such sera, although of doubtful value when given subcutaneously, might show valuable properties if applied in concentrated form at the very seat of infection.

Bacterial vaccines have been used in cerebrospinal meningitis with success by McKenzie<sup>11</sup> and by Rundle and Mottram,<sup>12</sup> but in the presence of such encouraging serumtherapy their use does not seem likely to be extensive. Unique is the experience of Radman,<sup>13</sup> who inoculated two patients subcutaneously with 8 c.c. of their own cerebrospinal exudate. No harm was done, and Radman thinks this form of specific therapy has a hopeful future.

**CHOLERA.** Haffkine<sup>14</sup> states that the incidence of the disease among the inoculated is one-tenth that of the uninoculated. The effect of the inoculation lasts fourteen months. If the disease is once contracted, however, the course and mortality is the same in the inoculated and the uninoculated. Effective antisera have not been developed.

**INFECTION DUE TO THE COLON BACILLUS.** Colon infections, especially those of the urinary tract, seem particularly favorable for vaccine treatment. Subjective improvement is oftentimes very striking. Pain and frequency of micturition are relieved quickly, and there is much general improvement. The character of the urine, however, changes but slowly, and complete elimination of bacteria from the urine is rare. Colon vaccines were used by Wright and Reid with success in two gall-bladder fistulæ after operation for gallstones. Vaccines have been used also with possible advantage after appendix operations.

**DIPHTHERIA.** Little new can be said on the subject of diphtheria antitoxin. It continues to be first and foremost of the anti-sera. The unbelievers become fewer every year. To the unconvinced, however, I would advise the study of a chart shown by Park in his Harvey lecture of 1905-1906. The mortality rate per 100,000 from diphtheria and croup in nineteen large cities of Europe, England, and the United States from 1878, to 1905, is here tabulated by years. The simultaneous reduction in the death rate from diphtheria and croup in all these widely separated cities since the introduction of antitoxin is most striking and gratifying (see chart).

The prophylactic benefits of antitoxin are well exemplified in a report of Terribile,<sup>15</sup> who made 2500 preventive inoculations in a recent epidemic. Of these, only 17 took the disease and none died. Comby<sup>16</sup> urges very strongly the use of frequent and large doses of

<sup>11</sup> Brit. Med. Jour., June 15, 1907.

<sup>12</sup> Lancet, July 27, 1907.

<sup>13</sup> Münch. med. Woch., July 4, 1907.

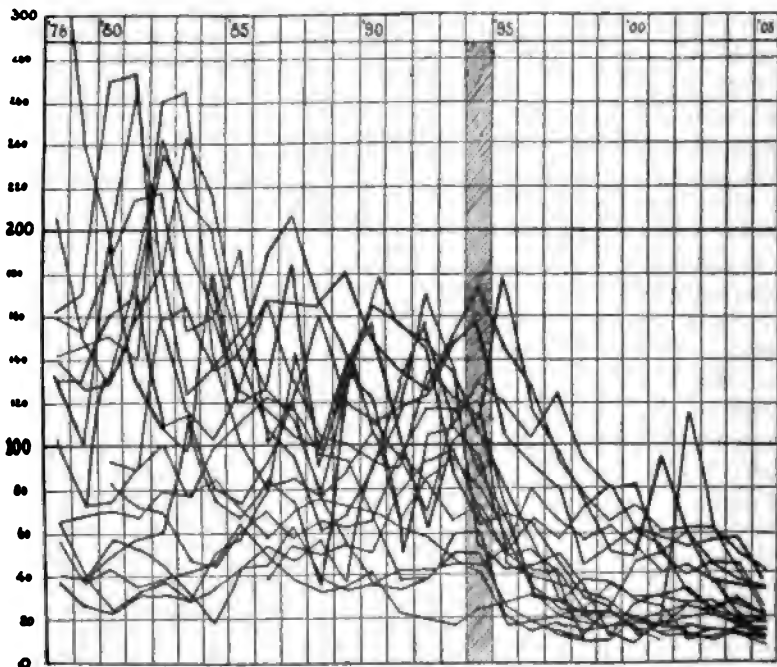
<sup>14</sup> Bull. de l'Inst. Pasteur, September 15 and 30, 1906.

<sup>15</sup> Gas. degli Ospedali, Milan, xxviii.

<sup>16</sup> Bull. med., Paris, 1907, 442.

antitoxin in case of diphtheritic paralysis, whether recent or old, light or severe, in child or adult. He repeats the injection every day for six days if necessary, and has cured all of 13 cases. Of these 13, 7 had antitoxin during the original disease, 6 had not. The methods of Park and his co-workers for the refinement of diphtheria antitoxin have been confirmed and very generally adopted.

For a number of years Emmerich and Løwe have claimed marked bactericidal and antitoxic properties for their filtrates of cultures of *Bacillus pyocyaneus*. Very recently Mühsam<sup>17</sup> has



Deaths per 100,000 from croup and diphtheria in nineteen large cities (1878-1905).  
(Park.)

investigated the substance, and substantiates in part the claims made for it. Experimentally, it does inhibit markedly the growth of diphtheria bacilli and many other bacteria. It seems also to neutralize in some way diphtheria toxin. Clinically the "pyocyanase" does no harm, and seems to digest the membrane in quite a remarkable manner. The fever is much decreased, and the general condition of the patient much improved. It is not to be used alone, but together with antitoxin.

<sup>17</sup> Deut. med. Woch., February 6, 1908.

**BACILLARY DYSENTERY.** Specific therapy has made a great deal of progress in this disease. Considerable confusion has arisen because of the varying types of bacillus found in different epidemics. The Shiga-Kruse variety has been found to be more virulent than the Flexner type and more efficient in the production of an antiserum. A polyvalent serum produced by inoculation with both types of bacilli has been suggested, and would seem to have the best outlook. The serum is both bactericidal and antitoxic. Good results cannot be expected unless the patient is injected with serum corresponding to the serum infecting organism. Bacteriological diagnosis is, therefore, very important, unless a polyvalent serum be available.

As to the efficacy of the serum, reports from Japan, Austria, France, Russia, and England agree in according it marked power. Shiga<sup>18</sup> treated 298 cases, with a death rate of 9 to 12 per cent. The length of the disease in those who recovered was twenty-five days; in those who died sixteen days. In 212 cases treated with drugs the mortality was 22 to 26 per cent. Those who recovered were sick forty days; those who died eleven days. In Russia Rosenthal gave serum treatment to 157 cases, with only 8 deaths—5.1 per cent.

Shiga inoculated 10,000 people in Japan with a mixture of dead bacilli and specific serum. The incidence of the disease was not much affected, but the mortality was reduced from 20 to 30 per cent. to practically nothing. Treatment of the original disease with specific vaccines has been tried in a few cases with success.

**ERYSIPELAS.** Schorer<sup>19</sup> treated 37 cases of erysipelas with streptococcic vaccines (4 strains). The disease was apparently shortened somewhat, but immigration or recurrence was not prevented.

**EXOPHTHALMIC GOITRE.** Bulkeley<sup>20</sup> reviewed all cases that had received specific treatment except those of Beebe and Rogers. This series numbered 86, of which 80 were benefited, 6 were not. In 16 cases the disease was probably cured. The substances used were thyroidectin, Moebius' serum, rodagen (dried milk powder of thyroidectomized animals), parathyroids of cows, milk of thyroidectomized goats, Murray's serum (animals fed with thyroid extract).

Beebe and Rogers<sup>21</sup> report 90 cases, of which 23 are regarded as cured, 52 improved, 11 not benefited, 4 died. Their serum, produced by intraperitoneal inoculation of Belgian hares with nucleoproteids and thyroglobulin from pathological and normal thyroids, exerts an antitoxic effect and also an inhibitory action upon cells of the glands.

Inasmuch as all writers agree that specific antithyroid therapy has been followed by beneficial results of greater or less degree,

<sup>18</sup> Osler. *Modern Medicine*.

<sup>19</sup> *AMER. JOUR. MED. SCI.*, 1907, cxxxiv, p. 728.

<sup>20</sup> *Boston Med. and Surg. Jour.*, 1907, p. 626.

<sup>21</sup> *Jour. Amer. Med. Assoc.*, September 1, 1906.

work along this line would seem to have a substantial basis, and much promise for the future.

**GONORRHOEA.** The treatment of the common infections of the urethra and conjunctiva by specific gonorrhoeal sera and vaccines has not, thus far, met with much success. In certain secondary involvements, however, the outcome is more encouraging. Rogers and Torrey<sup>22</sup> report a series of 98 gonorrhoeal joints treated with a polyvalent gonorrhoeal serum; 80 per cent. of the cases were cured or much improved; 20 per cent. showed slight or no improvement. Not much can be hoped for in chronic cases with structural changes in the joints. Porter<sup>23</sup> had similar favorable results in 7 cases of gonorrhoeal joints. He thinks the cases remarkably free from complicating disabilities. Moreover, the primary urethritis seemed to him to be favorably affected. Swinburne<sup>24</sup> was much impressed with the action of Rogers and Torrey's serum in 11 cases of gonorrhoeal epididymitis. In 2 cases treatment was instituted very early (in 8 cases within twenty-four hours) and the course of the disease seemed to be remarkably modified and shortened.

The use of specific vaccines in gonorrhoeal joints has been followed in most instances by favorable reports. Cole and Meakins,<sup>25</sup> in an experience with 15 cases, thought distinct benefit was conferred by inoculation. At the Massachusetts General Hospital Dr. H. F. Hartwell has treated 31 cases (as yet unpublished) with encouraging results. In a personal communication Dr. Hartwell says: "There were 31 gonorrhoeal joints, 14 acute, 17 subacute and chronic. In 11 cases the gonococcus was obtained from the urethra and grown in pure culture. In 3 cases cultures were made from the joint, with 1 positive result. In 14 acute cases, the average time from beginning treatment until resuming work was six to seven weeks; the shortest three, the longest twenty and one-half weeks. In addition to vaccines, they had fixation while the acute symptoms lasted, and some had baking and massage. All but 3 obtained complete motion in the affected joints; 2 of these were infections of the right wrist and hand, and in both motion in the wrist is limited by adhesions. In 1, an infection of the metacarpophalangeal joint, stiffness persisted. These 3 cases were treated with stock vaccine. In the 17 subacute and chronic cases disability in the joints had existed for periods varying from three weeks to two years. The average duration of treatment was 5.9 weeks, the shortest one and one-half, longest twelve and one-half weeks. In some cases passive motion on Zander machines was used. All were discharged with good functioning joints. One case, in addition to multiple subacute joints, had adhesions in both hips, the result of a previous infection. Treatment had no effect

<sup>22</sup> Jour. Amer. Med. Assoc., September 14, 1907.

<sup>23</sup> Jour. Royal Army Med. Corps, 1907, p. 513.

<sup>24</sup> Jour. Amer. Med. Assoc., 1907, 319.

<sup>25</sup> John Hopkins Hosp. Bull., June to July, 1907.

on adhesions. It seems doubtful if vaccines had any influence on shortening the acute symptoms, although the variation in the individual infection makes this difficult to determine. In chronic joints response to treatment was more obvious, and cases which had been obstinate for a long time seemed to clear up more rapidly under vaccine treatment. No appreciable effect was noted in lessening the urethral discharge."

Somewhat exceptionally Butler and Long<sup>26</sup> had marked success in the treatment of vulvovaginitis in children with gonorrhœal vaccines. Most of the cases had been doing badly on routine treatment. The results of vaccine treatment were much more sharp and definite. The patients' stay in the hospital was shortened. Two cases which had not improved on a monovalent vaccine, improved rapidly when a polyvalent vaccine was substituted.

Altogether, the outcome for specific treatment in gonorrhœa, in some of its phases at least, is distinctly hopeful. If vaccines will accomplish as much as sera, the question will, of course, be much simplified.

**HAY FEVER.** The report of Curtis<sup>27</sup> shows that there is anything but unanimity among specialists as to the therapeutic value of pollantin. Curtis says that "in response to 300 inquiries of specialists, the great majority states that, without the removal of ridges, spurs, etc., the treatment has been unsatisfactory." Knight,<sup>28</sup> on the other hand, who collected 219 cases from 81 physicians, found that 52 per cent. of the cases were effectively benefited; 30 per cent. partially benefited; 18 per cent. not benefited.

**LEPROSY.** In an effort to influence favorably the course of leprosy a number of different substances have been made use of. Among these may be mentioned tuberculin, diphtheria antitoxin, anti-snake venom, and sera produced by inoculation into animals of ground-up leprosy nodules.

More recently Rost,<sup>29</sup> of the Indian Medical Service, has inoculated 124 cases with the filtrates of a six-months-old culture of the leprosy bacillus upon a special medium. Fourteen cases have been cured. The others have shown marked improvement.

Deycke<sup>30</sup> has isolated from leprosy nodules what he calls *Streptothrix leproides*. Extraction of this with ether gives a neutral fat which he calls "nastin." Combined with benzoyl chloride, nastin becomes much more powerful, and injected into patients causes a reaction quite similar to the tuberculin reaction. After inoculations the lepra bacilli in the nodules show marked degeneration and bacteriolysis. Results upon 40 patients give Deycke much encouragement.

<sup>26</sup> Jour. Amer. Med. Assoc., March 7, 1908.

<sup>27</sup> Ibid., July 13, 1907.

<sup>28</sup> Ref. to by Dyer, Osler's Modern Medicine.

<sup>29</sup> Med. Record, March 10, 1906.

<sup>30</sup> Brit. Med. Jour., April 4, 1908.

**LEUKEMIA.** Samson<sup>31</sup> reports a case of a child with lymphatic leukemia, in which the leukemic signs and symptoms completely disappeared during an intercurrent attack of noma. After the subsidence of the noma, however, the leukemic condition recurred and the child died.

Larrabee<sup>32</sup> has treated 4 cases of leukemia with the mixed toxins of streptococcus and *Bacillus prodigiosus* (Coley). The first case was that of the splenomyelogenous type and was greatly improved. Of three lymphatic leukemias, one was slightly improved and two not improved.

Personally, I have used these toxins in one case of lymphatic leukemia in its last stage. Coincidentally with the inoculation the glandular enlargements decreased, as did also the size of the spleen. The blood picture also improved a good deal. The patient, however, lost strength steadily, and finally succumbed to an intercurrent pneumonia.

**PLAGUE.** Haffkine<sup>33</sup> states that among 639,630 uninoculated persons there occurred 49,433 cases of plague (7.7 per cent.), with 29,733 deaths (4.7 per cent.). Of 186,797 who had been inoculated with plague vaccine, 3399 (1.8 per cent.) took the disease and 814 (0.4 per cent.) died. Production of immunity is quite rapid; so much so that Haffkine believes that vaccines used very early in the disease can be of service in aborting it. As to serum treatment, Bannermann and Terni compared 1014 cases treated with four kinds of serum with 1020 untreated cases, and found the mortality practically the same. Early treatment is very important. Choksy, who has had large experience, had, in private practice, a death rate of 40 per cent., as compared with 62 per cent. in hospital cases which came under treatment on the average much later.

**PNEUMONIA.** Anti-pneumococcic serum has been used by a number of clinicians here and abroad. Individuals have been enthusiastic in its praise, but the consensus of opinion is against its having any marked therapeutic value. Treatment with specific vaccines has been tried by Wolf<sup>34</sup> in 14 cases, with 3 deaths (27.2 per cent). The mortality in untreated cases for the same epidemic was 40 per cent. Vaccination was followed by rise in the opsonic index, and crisis occurred in those who recovered within eighteen hours in all cases except one. Five cases had crisis on the third day; 3 on the fourth; 1 on the fifth; 2 on the sixth day. Further investigation along these lines would seem to be indicated.

Empyema due to the pneumococcus has seemed in the hands of a number of observers to be especially amenable to vaccine treatment.

<sup>31</sup> Berl. klin. Woch., February 3, 1908.

<sup>32</sup> Boston Med. and Surg. Jour., February 6, 1908.

<sup>33</sup> Bull. de l'Inst. Pasteur, October 30, 1906.

<sup>34</sup> Jour. Infect. Dis., 1906, p. 739.

**SARCOMA.** Coley,\* in his recent report on the treatment of sarcoma with the toxins of streptococcus and *Bacillus prodigiosus*, says that to date, in 47 personal cases and 100 of other surgeons, the tumors have completely disappeared. In 28 personal cases and 30 of other physicians there has been no recurrence for a period of three years. Among his personal cases there were sarcomas of every kind but melanotic. In a majority of instances the diagnosis was confirmed by pathologists of the first class.

**STAPHYLOCOCCIC INFECTION.** As is well known, results in staphylococcic infections treated with specific vaccines have been more encouraging than in any other variety of bacterial invasion. Opinion is practically unanimous that acne, boils, carbuncles, sycosis, fununculosis, etc., are very favorably influenced. Whether general blood invasion with its high mortality can be controlled remains to be seen. Early blood cultures must become, in these cases of general sepsis from whatever germ, more a matter of course, for in this way only do early diagnosis and early specific treatment with autogenous vaccines become possible.

**STREPTOCOCCIC INFECTIONS.** The question of streptococcic infections, sera, and vaccines is still very confused. The differences in race and virulence of various streptococci makes the study of immunity most difficult. In all the discussions, however, polyvalence, be it of serum or vaccine, is an acknowledged point of great importance. Treatment, furthermore, must be begun at the earliest possible moment. Statistics are unsatisfactory, but the general impression is that specific therapy does good. Generally speaking, local infections have done the best.

The recent literature shows, however, a number of cases of general streptococcic sepsis treated successfully with autogenous vaccines. No harm has been done apparently, and the method should surely be tested.

Most interesting and encouraging has been the study on scarlet fever and its relation to the streptococcus. Work by Gabritschewsky and other Russians has emphasized the important role played by the streptococcus in scarlet fever. They point out that the streptococcus is present in many scarlet fever throats; that streptococcus vaccines cause scarlatiniform eruptions; that complement deviation shows streptococcus amboceptors in scarlet fever blood; that the mortality in scarlet fever has been markedly reduced by the use of a serum produced by inoculation of a scarlet fever streptococcus (Moser); and finally, that by inoculation of streptococcus vaccines efficient prophylaxis against scarlet fever has been secured.

**SNAKE VENOMS.** Early in his studies upon snake venoms and their antidotes Calmette thought that anticobra serum would be efficient against other venoms as well. More recent work, however,

\* *Bost. Med. and Surg. Jour.*, February 6, 1906.

by Lamb, also by Flexner and Noguchi, has shown that antivenoms are highly if not absolutely specific. To be of any practical value, therefore, a protective serum will have to be polyvalent.

**TETANUS.** There is practically no dissent from the view that tetanus antitoxin is all powerful in prophylaxis. It must be given as early as possible. The greater the delay the larger the dose should be. As to treatment of the declared disease opinions differ. One observer has said that "light cases get well without serum, and severe cases die with it."

Brandenstein<sup>26</sup> treated 20 cases with serum subcutaneously, with 16 deaths—mortality 80 per cent. Hoffmann<sup>27</sup> treated 13 cases subcutaneously, with 7 deaths—53.8 per cent. Of 16 cases, however, in which serum was injected intradurally, only 2 died. One of these died from a complicating pneumonia. The other was very weak after amputation of an arm for sarcoma, and would have died anyhow in all probability. Discarding these 2 cases, Hoffmann has, with intradural inoculation of serum, a clean slate of 14 cases with no deaths.

**TUBERCULOSIS.** Through ignorance of its dangers, specific therapy in tuberculosis received in its infancy a setback which it has taken years for it to recover from. Gradually, however, its laws and limitations have become better known and its great value is now recognized the world over. The favorable opinion refers now especially to active immunization produced by direct inoculation of the tubercle bacillus or its products.

It makes little difference apparently what variety of tuberculin is used. More depends upon the method and skill of the physician. Inasmuch as, in animal experimentation, inoculation with the living bacillus produces the strongest immunity, we should, theoretically at least, aim to approach, as nearly as possible, these conditions in human treatment. This would be secured approximately by a combination of living filtrate (Tuberculin B. F. of Denys) with bacillary emulsion (Tuberculin B. E. of Koch). Corresponding tuberculins of the bovine type are much used by Spengler, who claims that there is a mutual antagonism between the two varieties of bacilli and their pathological processes. Thus, he says, pulmonary tuberculosis is the result of infection with the human types of bacillus and must be treated with bovine tuberculin, whereas, tuberculosis of bones, joints, and glands, being due to bovine bacilli, is best treated with human tuberculin. Be that as it may, bovine tuberculins may be tried in those cases which do not improve on the human varieties.

The whole question of tuberculin treatment has been much clarified through the work of Denys and Trudeau, and has been well summed up by Ringer in the dicta that "time and tolerance" are the essential things, and that the word "haste" has no place in treat-

<sup>26</sup> Deut. Zeit. f. Chir., vol. xcii.

<sup>27</sup> Beil. für klin. Chir., October, vol. lv.



ment with tuberculins. Although in the past a careful selection of cases for tuberculin treatment has been deemed essential, the opinion seems to grow that practically any case can be inoculated if sufficient care be exercised.

Allen<sup>38</sup> has recommended in tuberculosis a vaccine made from tuberculous sputum. Such a vaccine has a number of theoretical advantages. It is a mixed vaccine, contains primary and secondary invaders, the bacteria concerned are autogenous, and their fighting powers have not been diminished by artificial cultivation.

Specific antisera have been used especially in Europe. The best known are those of Marmorek and Maragliano. Opinions of these in their own countries have been, on the whole, favorable, but as tried in this country, at the Phipps Institute and at Saranac, the results have shown them to be of doubtful value.

**TYPHOID FEVER. Prophylaxis.** As a result of specific inoculation of large numbers of troops in the British Army the following results were obtained by Wright: Of 1758 inoculated, 142 died (8 per cent.). Of the uninoculated, of whom there were 10,980 under the same general conditions, 1800 died (16.6 per cent.). The incidence of the disease in the various squadrons was anywhere from two- to twenty-eight-fold greater in the uninoculated than in the inoculated. As an inoculating fluid Wright used dead cultures. Two doses should be given to secure the best results. The only disadvantage of the procedure seemed to be that inoculation is followed by a short period of hypersusceptibility to infection. Increased immunity seems to last from one to three years.

The experience of the Germans with antityphoid inoculation has not been so extensive, but in the main confirms Wright's results.<sup>39</sup> Of 424 typhoids, 324 had not been inoculated. In the uninoculated the mortality was 11.9 per cent.; in the inoculated, 4 per cent. In the inoculated the disease was milder and there were fewer complications and relapses.

In the treatment of typhoid fever no one has approached, in experience or success, Chantemesse<sup>40</sup> in Paris. With his colleagues he has treated 1000 cases, with a death rate of 4.3 per cent. Of 5621 cases who were given routine treatment during the same period, 17 per cent. died. Of patients who were given serum treatment before the seventh day Chantemesse lost not a single one. The nature of Chantemesse's serum is difficult to understand. He speaks of it as antitoxic and as produced by inoculation of horses with a true typhoid toxin. It does not, however, act directly upon the toxin, as does the diphtheria antitoxin, but in some way indirectly. It stimulates the spleen, bone marrow, and other lymphatic apparatus

<sup>38</sup> Jour. Amer. Med. Assoc., July 20, 1907.

<sup>39</sup> See Morgenroth in Kolle u. Wassermann's Handbuch der pathogenen Mikro-organismen. Ergaenzung's Band, No. 1, S. 234.

<sup>40</sup> Hygiene gén. et appliqué, Paris, 1907, 577.

to increased opsonin production. The sicker the individual the smaller must be the dose, lest too many bacilli be destroyed at once. There would seem to be, therefore, a strong bactericidal element in the serum. The serum treatment is combined with the cold bath treatment, and calcium chloride is given as a routine measure to prevent hemorrhage. Chantemesse's results have been confirmed to a certain extent by the Germans, and von Leyden<sup>41</sup> reports 3 cases treated with antitoxic serum prepared by Meyer and Bergell.<sup>42</sup> These cases were all remarkably short, having normal temperatures on the sixteenth, seventeenth, and nineteenth days. The serum is said to be of only moderate strength and to be both bacteriolytic and antitoxic. In this connection it is important to bear in mind, as suggested by von Stenitzer, that an antitoxin, although weak, as in dysentery, may be of great service in tiding over critical cases.

Personally, I have treated 132 cases of typhoid fever with specific typhoid products,<sup>43</sup> serum, bouillon filtrates, and the non-toxic residue of the typhoid bacillus as prepared by Professor Vaughan, of Ann Arbor. The results were largely negative, with one exception. By continued inoculation during convalescence of the non-toxic residue the occurrence of relapses was cut down apparently from 22 to 5 per cent.

Very recently I have treated 2 cases with autogenous vaccines. One case was quite severe, with marked mental and renal involvement. He received about 40,000,000 dead bacilli daily under the skin for two and one-half weeks. There was steady though slow improvement. The second case was the earliest and mildest I have ever seen. Daily inoculations with 25,000,000 to 50,000,000 autogenous vaccines was followed by rapid fall in temperature, which reached normal on the sixteenth day. This case emphasizes the fact that in typhoid, as in other infectious processes, specific treatment, to be effective, must begin early. Hospital cases, in my experience, do not come in on the average until the end of the second week. Lack of positive diagnosis also entails oftentimes further delay.

In the future, however, with the more general use of blood cultures, early diagnosis and earlier specific treatment will be possible, and the results, I am sure, better.

Theoretical considerations and personal experience lead me to believe that in any treatment of typhoid fever with bacterial products (and this idea applies to other infectious processes as well) we might get more favorable results if we combined dead bacilli with the filtrate of living cultures, for such a combination would approximate more nearly to inoculation with the living organism.

I have found typhoid patients infinitely more sensitive to living filtrates than to any of the devitalized bacillary substances, and I

<sup>41</sup> Med. Klin., August 4, 1907.

<sup>42</sup> Berl. klin. Woch., May 6, 1907.

<sup>43</sup> Boston Med. and Surg. Jour., October 3, 1907.

feel certain that the degree of heat necessary to kill the bacilli destroys other products of growth which may be very essential to the production of rapid immunity.

This point is, of course, not new. It has already received attention in tuberculosis, in the recommended use of tuberculin B. F. either alone or combined with tuberculin B. E.

As to the value of the opsonic index as a guide for the use of vaccines, the opinion has steadily gained ground that the index is so unreliable as not to justify the amount of time and trouble necessary for its determination.

### THE PARAVERTEBRAL TRIANGLE OF DULNESS (GROCCO'S SIGN) IN PREGNANCY.

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It has been satisfactorily demonstrated by Grocco,<sup>1</sup> Rauchfuss,<sup>2</sup> Thayer and Fabyan,<sup>3</sup> Ewart,<sup>4</sup> Frankenheimer,<sup>5</sup> and others that when there is a collection of fluid in one pleural sac dulness on the opposite side of the spine may be percussed. This dulness is roughly of triangular outline, and is so placed that the spinal column forms its vertical side. It has also been frequently demonstrated that in conditions other than simple collections of fluid in the pleural sac paravertebral dulness may be obtained. This is particularly the case in lobar pneumonia, when the consolidation lies along or near the spine, and in various newgrowths when the tissues of the mediastinum are involved. The paravertebral area of dulness in these cases rarely has the distinct triangular form that is so well marked in pleural effusion. Other characteristics, such as variations in size and shape of the paravertebral dulness, voice and breath sounds over and adjacent to the triangle, etc., may be wanting.

Recently several observers have reported cases in which it was possible to obtain a paravertebral dulness in conditions in which the affections were extrathoracic. Ewart<sup>6</sup> mentions that dulness may be percussed along the spine in ascites; Beall<sup>7</sup> gives details of a well-delimited paravertebral triangle on the left side in a case of subphrenic abscess, and a short time ago I called attention to

<sup>1</sup> Rivista crit. di clinica med., 1902, Nos. 13 and 14.

<sup>2</sup> Deut. Archiv f. klin. Med., 1906, lxxxiv, 186.

<sup>3</sup> Amer. Jour. Med. Sci., January, 1907.

<sup>4</sup> California State Jour. Med., 1907, v, 224.

<sup>5</sup> Jour. Amer. Med. Assoc., 1907, xlix, 2148.

<sup>6</sup> Lancet, 1907, ii, 49, 189.

<sup>7</sup> Lancet, 1907, ii, 189.

Grocco's sign in a patient whose affection proved to be an enormous multilocular cystadenoma in the abdominal cavity.<sup>8</sup>

The presence of paravertebral dulness in this case of cystadenoma suggested to me that similar areas of dulness might be obtainable in cases in which the abdominal tumor was not pathological, as in pregnancy. Through the courtesy of Dr. Frank C. Witter, of the University of Michigan Maternity, service of Professor Reuben Peterson, it has been possible to record observations upon seven cases with fairly well-marked abdominal tumor. A few details concerning each case may prove of value:

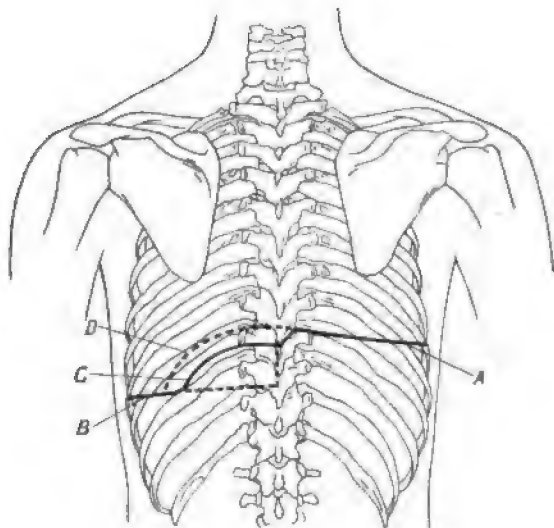


FIG. 1.—A, upper border of the liver; B, lower limit of the thoracic resonance; C, paravertebral dulness—patient upright; D, paravertebral dulness—patient leaning to the left.

CASE I.—Primipara, aged eighteen years, rather slender, eight and one-half months pregnant. There is moderate abdominal tumor when the patient is sitting; the patient "carries" rather high. The thorax is negative. Posteriorly the liver is at the ninth rib, in the right midscapular line (Fig. 1); the spinal dulness is just below the eighth dorsal spine; the lower limit of thoracic resonance on the left is in the midscapular line, at the tenth rib. To the left is a well-delimited area of dulness lying along the spine. Its base at the level of the tenth rib measures 7.5 cm. out from the midvertebral line; its vertical height is about 2.5 cm. The hypothenuse of the area is convex outward, and is rather more so toward the base. When the patient leans sharply to the left, the base is 9 cm. long and the spinal dulness 5 cm. There are no changes when the patient leans to the

<sup>8</sup> Jour. Amer. Med. Assoc., 1908, II.

right. There are no auscultatory signs over the paravertebral area nor over the adjacent lung.

**CASE II.**—Primipara, aged sixteen years, medium build, eight months pregnant. The abdomen is moderately large when sitting. The thorax is negative. Posteriorly the liver is at the ninth rib in the right midscapular line (Fig. 2); spinal dulness is at the ninth thoracic vertebra; on the left the lower limit of thoracic resonance is at the ninth space in the midscapular line. A rather flat-topped area of dulness may be percussed to the left of the spine. Its base at the level of the ninth space measures 7 cm. from the midvertebral line; its elevation on the spine measures 2.5 cm. There are no demonstrable changes in shape or size of the paravertebral dulness when the patient changes position. Auscultation is negative.

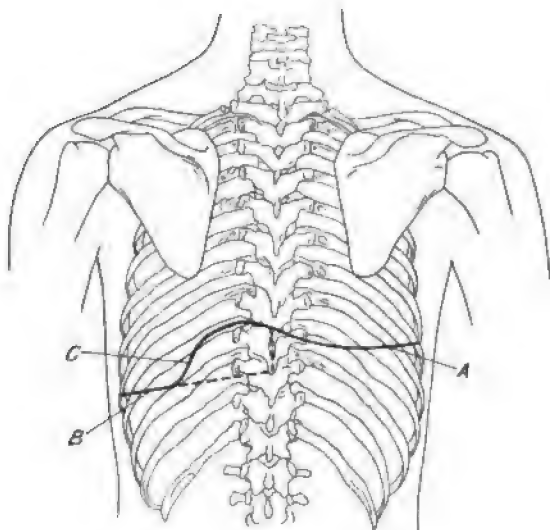


FIG. 2.—A, upper border of the liver; B, lower limit of the thoracic resonance; C, paravertebral dulness—patient in any position.

**CASE III.**—Primipara, aged twenty-one years, of slender build. She is overdue about fifteen days. When sitting erect she has a moderately prominent abdomen, the greatest prominence being low down. Occasionally she has weak pains. The thorax is negative. Posteriorly the liver is at the ninth space in the right midscapular line (Fig. 3); the spinal dulness begins at the tenth thoracic spine; the lower limit of thoracic resonance on the left follows the tenth rib. *There is no area of dulness along the spine on either side, whatever position the patient may assume.*

**CASE IV.**—Primipara, aged nineteen years, of very slender build, about one and one-half weeks from term. The abdominal distention is rather high when the patient is sitting. The thoracic

examination is negative. Posteriorly the liver dulness is at the tenth rib in the right midscapular line (Fig. 4); the spine is dull at

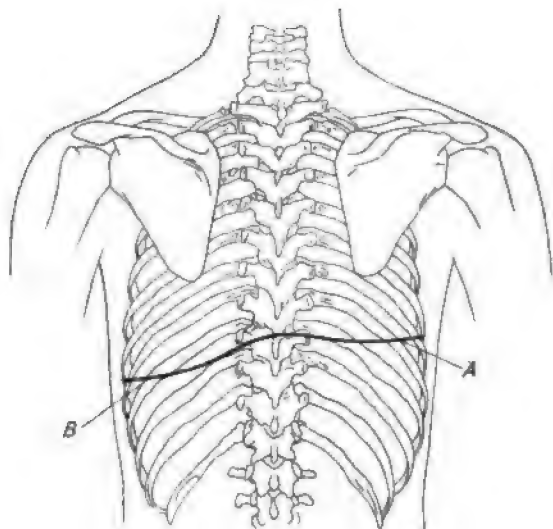


FIG. 3.—*A*, upper border of the liver; *B*, lower limit of the thoracic resonance.

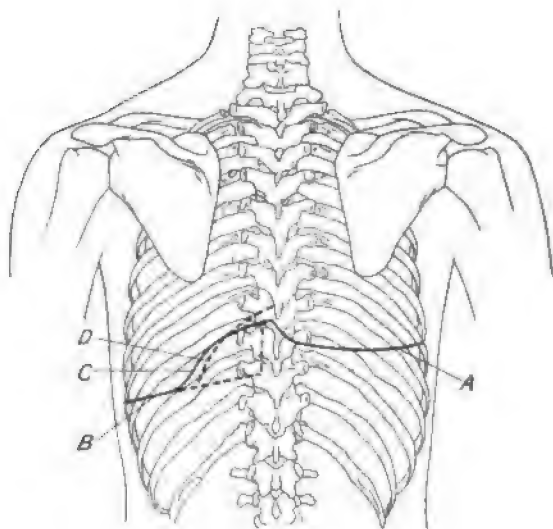


FIG. 4.—*A*, upper border of the liver; *B*, lower limit of the thoracic resonance; *C*, paravertebral dulness—patient upright; *D*, paravertebral dulness—patient leaning to the left.

the ninth thoracic spine; the lower border of thoracic resonance on the left is at the tenth rib in the midscapular line. A sharply defined area of dulness, roughly of triangular outline, may be made

out to the left of the spine. Its base extends 8.5 cm. from the mid-vertebral line; its elevation at the spine is 2.5 cm. When the patient lies on the right side the area shows no marked change; when she lies on the left, the base measures 7.5 cm., and the elevation at the spine is 4.5 cm. There are no auscultatory signs over the triangle or the adjacent lung.

CASE V.—Primipara, aged nineteen years, of slender build, eight months pregnant. There is moderate abdominal distention when the patient is sitting. The thorax is negative. Posteriorly the liver is at the ninth space in the right midscapular line (Fig. 5); the spinal dullness begins at the ninth thoracic vertebra; the lower limit of thoracic resonance on the left is at the tenth rib in the mid-

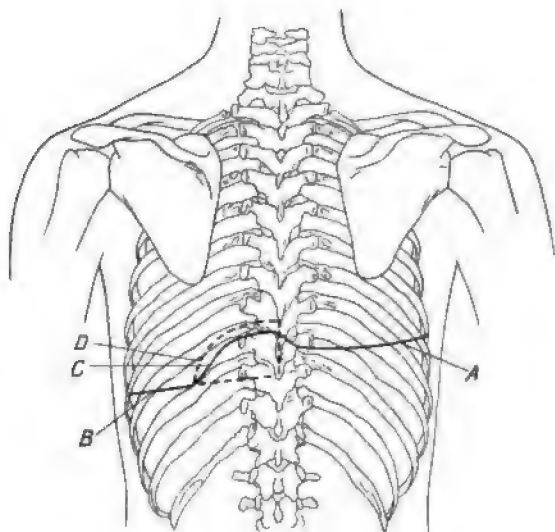


FIG. 5.—A, upper border of the liver; B, lower limit of the thoracic resonance; C, paravertebral dullness—patient upright; D, paravertebral dullness—patient leaning to the right.

scapular line. An area of paravertebral dullness can be made out to the left. Its base at the level of the tenth rib extends out from the midvertebral line for about 4.5 cm.; its elevation on the spine is 2.25 cm. The area is triangular, and its hypotenuse is moderately convex outward. When the patient leans sharply to the right the base of the triangle measures 4 cm., and its elevation 3.5 cm. When the patient leans to the left a like distance, the base measures 6 cm., and the elevation on the spine is 4.5 cm. There are no auscultatory signs.

CASE VI.—Primipara, aged twenty years, of medium build, about six months pregnant. There is a fair-sized abdominal tumor for the months pregnant. The thorax is negative. Posteriorly the liver is at the ninth space in the right midscapular line (Fig. 6); the

spinal dulness is at the tenth dorsal spine; the lower limit of thoracic resonance follows the tenth rib. *There is no paravertebral dulness on either side of the spine, whatever position the patient assumes.*

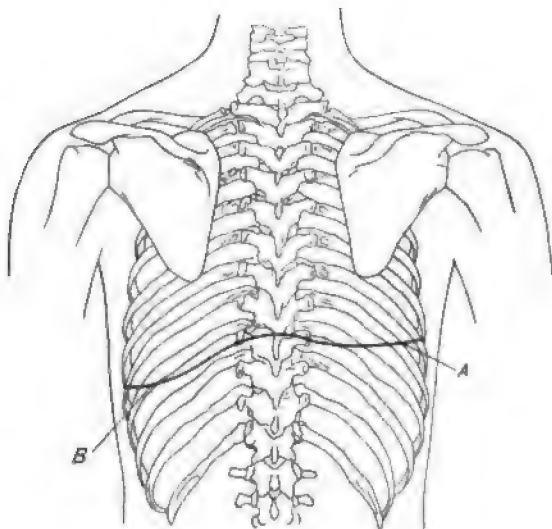


FIG. 6.—A, upper border of the liver; B, lower limit of the thoracic resonance.

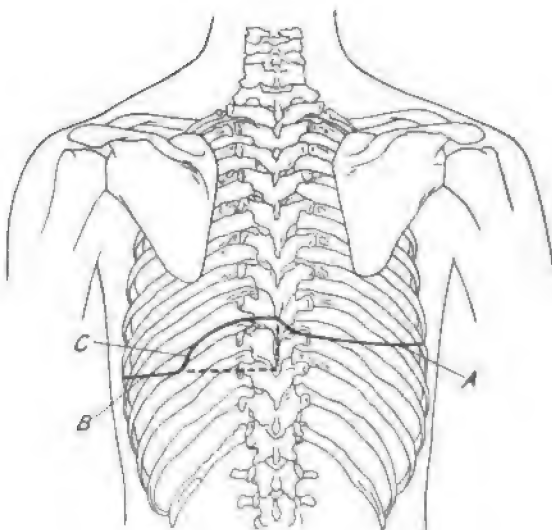


FIG. 7.—A, upper border of the liver; B, lower limit of the thoracic resonance; C, paravertebral dulness.

**CASE VII.**—Primipara, aged twenty-two years, strongly built, eight months pregnant. There is a moderate abdominal tumor when



sitting. The thoracic examination is negative. Posteriorly the liver is at the ninth rib in the right midscapular line (Fig. 7); the spinal dulness begins just below the ninth thoracic spine; the lower limit of thoracic resonance on the left follows the tenth rib. To the left of the spine is a flat-topped area of dulness lying along the spine. Its base measures 6.5 cm.; its elevation on the spine is 2 cm. There is no change when the patient leans sharply to the right; when she leans to the left the area appears rather larger, but not so noticeably so as to make accurate percussion possible through the rather thick parietes.

While the evidence herewith presented is rather scant, yet certain interesting and instructive points are well brought out. The patients were all primiparæ, with ages ranging from sixteen to twenty-two years. Five were pregnant between the eighth and the tenth month, one was about fifteen days overdue, and one was pregnant at the sixth month. In only two of the cases did percussion fail to demonstrate a well-marked area of dulness along the spine. The dull areas were roughly triangular, with more or less convex hypothenuses; and they *were all to the left of the midvertebral line*. In all cases examination of the thorax was negative. The paravertebral areas of dulness were not so distinctly triangular in outline as those that are percussed in cases of simple effusion into the pleural sacs. The hypothenuses appeared to be more markedly convex than in cases of effusion, and there was a tendency for the paravertebral dulness to be flat-topped. In two of the cases the hypothenuses were at a rather higher level than the point at which the line met the spine. Moderately strong percussion strokes were used to delimit the dull areas. The triangles were generally larger when the patients lay or leaned to the left, and rather smaller, although sometimes higher, when the patients leaned to the right. There were no definite auscultatory signs over the areas of dulness or over the lung adjacent thereto.

There were two cases in which the paravertebral dulness could not be percussed on either side of the spine, in whatever position the patient was placed (Cases III and VI). In Case III the patient was about two weeks past term, and was having weak pains at the time of the examination. The uterus had descended, but the membranes were intact. In Case VI the patient was at the sixth month, and the abdomen was moderately distended, but rather low down, compared with the other cases examined. It will be interesting to note whether or not this patient develops a paravertebral dulness to the left later in her pregnancy.

The paravertebral dulness in pregnancy appears to be due primarily to the abdominal tumor. This doubtless displaces other viscera upward. The greater "give" on the part of the diaphragm is to the left, where no solid organ, such as the liver, is found to sup-

port the abdominothoracic partition. The mediastinal tissues may be displaced by this more than normally arched diaphragm, and the lung may be temporarily moved away from the spine. It does not seem entirely possible for pressure of the mediastinal tissues or of the abdominal viscera upon the vertebræ and transverse processes to produce the well-marked paravertebral dull areas noted in the cases furnishing the basis for this report. Yet one cannot altogether feel certain that the dulness percussed along the spine is brought about by a large, hernia-like protrusion upward of the abdominal viscera. The viscera most likely to be displaced are the liver, stomach, and intestine. While some of the dulnesses percussed give outlines which might lead one to suspect that the liver is the origin, yet, were this so, it is not easy to see how it would be possible for one to get such readily obtained differences in shape and size of the areas on change of the patient's position. The combination of the two factors—of displacement of mediastinal tissues and encroachment of abdominal viscera upon the thoracic cavity, as result of the demands of the gravid uterus for room—appears reasonable. It is significant that in Case III, in which the uterus had descended just before the onset of labor, no paravertebral area of dulness was obtained. Likewise, in Case VI, in which the patient was pregnant at the sixth month, and the abdominal tumor was not yet very marked, the spine was resonant as low as the limit of thoracic resonance on the left.

But a short time ago the statement was made by a well-known observer\* that in simple, pleural effusion Grocco's paravertebral triangle of dulness gave promise of being pathognomonic. The complication of right-sided effusion, with pregnancy at the eighth month, would be interesting, in so far as the signs on percussion were concerned. The fact seems all the more firmly established that only rarely do we find signs or symptoms of disease that are pathognomonic. All must be taken as contributing relative material to the complete clinical picture.

## THE EFFECT OF OVERCIVILIZATION ON MATERNITY.

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THIS paper has been suggested by a series of cases seen in private practice and in consultation which present features so largely at variance with text-book obstetrics and with cases seen in hospital

\* *Progressive Medicine*, 1907, iii, 40.

practice, that the conclusion seems inevitable that a type of woman formerly very rare is now becoming relatively common, and that from the standpoint of the obstetrician special attention must be given to each individual case in order to give proper care at the time of labor. At first these variations from the normal were thought to be due to some personal idiosyncrasy on the part of the patient, and it was felt that no reason for their occurrence could be assigned except individual peculiarity, but an increased experience has led to the definite conclusion that, far from being occasional variations, the patients are members of an extensive class in the community, who furnish definite ground for the belief that under the increasing nervous and mental demands of the higher civilization which has been developed in our larger cities within a comparatively recent time, the overcivilized type of woman must receive special care during pregnancy and labor.

As time goes on the occurrence of these patients is becoming more and more frequent, and it therefore seems fair to assume that the conditions under which the girls of the present day are developed are growing worse rather than better, and that we must expect, in any large community at the present time, to find a considerable number of women, developed under the existing artificial conditions, who are widely separated from the normal type in many ways.

The development of this abnormal type in any community must have its effect on the practice of obstetrics in that community, because when a type unfit to bear the burden of maternity has been developed a new practice to meet the changed conditions is a necessity, if we are to preserve the life and health of this new class of patient. The effect of pregnancy and labor on the type of woman referred to can best be understood by brief quotations from the histories of several patients taken from actual experience, and then compared with the patients at the opposite end of the scale.

CASE I.—Mrs. C., aged thirty years; first pregnancy; bad neurasthenic history; always marked exaggeration of subjective symptoms whenever ill; prolonged attack of nervous prostration four years previously. Pregnancy normal throughout except for tendency to hysteria. Physical examination showed nothing abnormal. From the beginning of labor patient showed marked intolerance to pain and was extremely hysterical. First stage of labor lasted twelve hours, but in view of the utter lack of mental control on the part of the patient the second stage was terminated promptly by low forceps, as the patient was wearing herself out. A slight tear of the perineum was repaired; there was no abnormal hemorrhage. About an hour after delivery patient collapsed; complete mental prostration; poor pulse, which could always be counted at a rate from 130 to 150. Recovery from collapse was gradual, the condition becoming satisfactory at the end of about four hours. Convalescence from labor was normal except for exaggerated nervous symptoms.

CASE II.—Mrs. T., aged twenty-seven years; first pregnancy. Previous history: marked nervous sensibility, reacting excessively to slight impulse. Family history showed marked nervous tendency. Pregnancy fairly normal throughout except for the transient appearance of sugar in the urine at the seventh month. At the time of labor the patient was pale and anemic and in flabby muscular condition. She had refused to exercise during the last three months of pregnancy, partly on account of sensitiveness about her personal appearance, and partly on account of discomfort caused by walking. Considerable apprehension as to the outcome of labor. Physical examination negative. Labor from beginning was hard and painful, there being little interval between the uterine contractions. By the middle of the first stage of labor patient began to be markedly hysterical and showed a steadily rising pulse; she was etherized and delivered with forceps. Comparatively easy delivery, good ether recovery, no hemorrhage. Two hours after delivery sudden collapse appeared, with symptoms suggesting hemorrhage, but with no external hemorrhage present and no evidences of internal hemorrhage to be made out. Uterus acted well throughout. Collapse lasted four to five hours, and the patient gradually recovered under stimulation and morphine. Convalescence was slow and complicated by increased nervous symptoms. Patient was unable to nurse.

CASE III.—Mrs. G., aged twenty-four years; first pregnancy. Previous history: always well up to two years before marriage, when she broke down; had had a bad attack of nervous prostration, which lasted a year. During last six months was treated in a sanitarium. On leaving sanitarium was taken abroad for a year; was married shortly after her return to this country; became pregnant three months after marriage, first sign of pregnancy being marked nervous manifestations, which increased constantly during the pregnancy, until at the time of labor patient was in a marked melancholic condition. When labor began, the mental symptoms increased, and patient reacted badly to the pain of labor. Labor cut short by manual dilatation and delivery with forceps, four to five hours being the interval between the beginning of labor and delivery. Convalescence complicated by marked melancholic tendencies, from which the patient gradually recovered. A year afterward she was heard from, still in an unsatisfactory nervous condition, from which she has since slowly recovered.

The three patients whose history has been briefly given belong to a distinct and, in my experience, an increasing class which has been developed under the strain of existence in our large cities. This class of patients brings into the practice of obstetrics an element which is only occasionally referred to in obstetrical literature and never discussed in the text-books. The obstetrician whose practice lies among two distinct classes of patients, the one seen in hospital practice being largely composed of women of foreign birth, who

have not been subjected to the action of the influences brought to bear by the high requirements of modern civilization, and the other in his private practice, who have been subjected to those influences, must realize that he is dealing with two distinct types of women. As his experience with the civilized woman increases he must also realize that for a process which has been taught from time immemorial to be physiological, either great variations from the normal are possible in individual cases, or that differences in class and environment have developed new conditions which must eventually necessitate the development of a new method of procedure in order to obtain good results.

In the woman of the hospital type we see a patient who, in spite of the unfavorable conditions of her bringing up, poor food, privations, and hard work, comes to maturity a strong healthy woman, usually in absolute ignorance of the troubles incident to the highly developed nervous temperament. On the other hand, the overcivilized woman, brought up with every care and luxury, with little to do except to amuse and take care of herself, not infrequently arrives at maturity a delicate weakly specimen, whose nervous organization seems to overshadow and control her whole physical life.

When we study the two types in pregnancy and labor we find the differences equally well marked. The working woman, on the one hand, goes through her pregnancy with little or no trouble. In spite of her poor surroundings and the physical work which she is compelled to perform, even up to the advent of labor, or perhaps because of them, she ordinarily comes to labor, except in the presence of definite organic disease, in good physical condition to endure the strain, and goes through perhaps a hard labor without reacting unduly either to the pain or the muscular effort which she undergoes, and usually without aid of anesthetics delivers herself safely. She is ordinarily able to nurse her own child, and if she receives proper care in the repair of lesions and lacerations of childbirth, with an opportunity to rest until the generative organs have returned to a comparatively normal condition, she shows little or no effect of the strain which she has undergone, and is able to take up almost immediately the burdens of her ordinary life, with the addition of the care of her child.

The overcivilized woman, on the other hand, in spite of the fact that she receives constant attention throughout her pregnancy, is often the source of great anxiety to her attendant on account of the marked reaction which she often develops under the new strain which is imposed upon her. With her the nervous symptoms are the ones which are most likely to be exaggerated. Not only are symptoms of faulty elimination and auto-intoxication of greater or less degree relatively much more common than among the patients of the other class, who receive no care or attention, but she is likely to be unduly sensitive to outward influences and minor discomforts,

and is, therefore, often unwilling or unable to obtain the fresh air and exercise necessary to enable her properly to undergo the strain of labor. She often comes to labor, therefore, in a condition physically unfit to withstand any serious strain, and is not uncommonly so apprehensive as to the outcome of labor that her nervous equilibrium is often entirely lost. Throughout labor the nervous symptoms predominate, and pain even of moderate degree is apt to be endured badly and to cause an undue amount of exhaustion, both nervous and physical, for the amount of pain suffered. In spite of the use of anesthetics, labor is often pathologically painful, and not uncommonly a short and easy labor, terminated either normally or by an easy operation, undertaken to save the patient's strength, is followed by an alarming collapse from which recovery is likely to be very slow.

The convalescence is apt to be long and unsatisfactory, and it is not uncommon to find that six months or a year must elapse before the patient is restored to her normal health. The physical recovery may be complete and normally rapid, but it is the nervous breakdown with which we have to reckon, and even after convalescence is completed the patient is not uncommonly left with a dread of future pregnancies, amounting almost to a nightmare, a condition which should be definitely abnormal, but is unfortunately too common at the present time to be classed as an abnormality. Nursing among this class of patients may be considered one of the lost arts, and it is comparatively seldom that the patient is a satisfactory wet nurse, the common history being either that the milk proved to be unfit food for the child, or insufficient in amount.

▷ In a fair proportion of cases, however, the mother is able to nurse satisfactorily for a time, and then nursing has to be given up, either because the mother is showing the effects of the drain on her system, and is not convalescing properly, or because the breasts only function properly for a short time. In my experience three months is a longer time than the average patient of this class is able to nurse satisfactorily.

The contrast between these two types of patients is so marked that it seems impossible to believe that they have both gone through what is ordinarily considered a natural physiological process, and the conclusion seems inevitable that the conditions of civilized life are responsible for the increase of the unfit type of patient. These differences undoubtedly might in some cases be explained on the theory of evolution, and among the working classes the action of the principle of the survival of the fittest must be considered, the weaklings of the type being eliminated to a great extent during childhood. Among civilized women, on the other hand, the better conditions of their environment allow many of the weaker members, who for the good of the race should be eliminated, to reach maturity, and unquestionably, a certain proportion of the pathological material is drawn from these weaker members.

It seems to me, however, that the conditions above described are too prevalent to be explained on this hypothesis alone, and when we study the conditions under which girls, who, for convenience, are classed as the overcivilized type, are developed, it seems to me that in these conditions will be found the real key to the situation.

The city-bred girl of today is so carefully shielded from the undesirable features of her surroundings that she is brought up much as a hot-house plant. The conditions of her life and the mental and social development necessitated by the conventions of society, in which she is being educated to take her place, are such that a natural physical development is impossible, and from an early period of her life her hereditary tendency to an unstable nervous organization is constantly being increased by her education. The conditions under which she lives are such that the outdoor freedom necessary for her proper development is impossible. From the time when she is ten or twelve years old, or perhaps even younger, her education is being pursued with one definite object in view: she must be brought out as a finished, accomplished product, within a specified time, say at from seventeen to nineteen years of age, and certain definite accomplishments are considered essential to fit her for the life to which she is expected to devote a greater part of her time when she has entered society. For this reason, during the years she should be attaining her physical development under the best conditions of fresh air, outdoor life, and exercise, with a minimum degree of mental strain, she is compelled to conform to definite rules. She must be educated according to a certain arbitrary standard, whether suited to her mental capacity or not, and she is made to feel very strongly the disgrace of falling behind her friends. In this way the strain of competition is added to the mental strain already induced, and the burden is distinctly increased. Whether she has any aptitude or not, a certain training in music is considered a necessary part of her education, and it is not at all uncommon for a girl who is in school all the morning to spend a large part of the afternoon either preparing her lessons for the next day or in practising her music lessons.

In addition, dancing is one of the absolutely necessary requirements, and although the exercise which it necessitates is distinctly a benefit, it takes just so much time which could be devoted to gaining health in the open air, and adds another element of strain. In other words, her life is so full of gaining what are considered the necessary requirements of the civilized woman that she has comparatively little time, even if her surroundings furnished the opportunity, which they seldom do, for a healthful and outdoor life, but is constantly under a more or less severe nervous strain, and this at a time when her whole mental and physical organization is undergoing a complete change.

When she is finished and launched on her social career conditions become worse rather than better, for the hours are late and the social

engagements many and not to be neglected. If she has a taste for athletics and likes out-of-door sports, the time which she has to devote to her golf, tennis, and riding must be taken from the time when the girls of a non-athletic generation were resting after a late ball, and although the outdoor exercise is unquestionably a benefit, the time which can be devoted to it has to be taken from time which is needed for recuperation from the strain of her social obligations, and thus, particularly if her interest runs toward competitive athletics, a new burden is added rather than relief afforded. The result of this life is, in my opinion, very definite, and a large and increasing proportion of the girls who are subjected to this course of training suffer from a more or less complete nervous breakdown before they reach the age of twenty-five, and are temporarily nervous invalids at the time when their health should be at its best.

It seems to me that this overdevelopment of the nervous organization is responsible for the increased morbidity of pregnancy and labor which is apparent among these women of the overcivilized class. It may be, and apparently is, under the existing conditions, unavoidable, but unless the standard of feminine accomplishments changes, and so long as girls are subjected to a strain which would break down the constitution of the average man, with their ambitions aroused not to fall behind their quicker companions, we must expect to see a constantly increasing difference between the women brought up to lead natural lives and those who belong to the overcivilized class. As time goes on, therefore, it is inevitable that unless some change takes place, the changed conditions which have arisen must become generally recognized, and a new obstetrics must be formulated to meet the new conditions. That certain members of the profession have recognized the necessity for a change in the practice of obstetrics as heretofore carried out is evidenced by papers recently published, notably those of Reynolds and Davis, advocating a method of procedure which until a very recent date must undoubtedly have been classed as heretical, and even at the present time, except to those who recognize the signs of the times, must seem absolutely false teaching.

Those whose work takes them among the patients of the smaller communities or the larger communities where overcivilization is comparatively of recent development, will unquestionably refuse to accept the truth of these observations; from their standpoint they are unquestionably correct, for never having had the opportunity to study such patients they naturally fall into the error of believing that such patients do not exist, and a man is naturally prone to disbelieve what he has never had the opportunity to see.

If, therefore, we admit that in certain communities a class of women has been developed who are unfit to bear the burdens of pregnancy and labor, but who nevertheless are subjected to the strain, the question must arise as to what methods of procedure in the care of these patients will give the best chance of a favorable



result. Distinct differences of opinion will of necessity arise between those in the medical profession who admit the development of this unfit class and those who deny its existence, and even among those who recognize present conditions the problem of how they can best be met is far from settled. The ordinary duties which are incumbent on the obstetrician are to conduct an obstetrical case to a successful conclusion with a living mother and a living child, but the point is often lost sight of that the obstetrician has a further duty, which is to bring his patient through her troubles in such nervous and physical condition that she will be able to assume the functions and duties which properly belong to her after her convalescence is completed. The question which must be solved in these cases is what is the best method of accomplishing this object. There are many cases in which the first two points have been met, but in which the mother has been left for months or years a nervous wreck, due to a blind adherence to the belief that because other women who have been fit to undergo the strain of pregnancy and labor, have come through successfully, she must be able to do the same.

It seems to me, however, that the time has come when we must recognize the fact that abnormal conditions, such as have developed in our older communities, must be met in an abnormal way if we are to do our full duty to our patients. It is unquestionably true that many of these patients whose health has been wrecked, at least temporarily, by allowing them to undergo a strain for which they were evidently unfitted, both physically and nervously, would have been saved much suffering if the conditions present had been recognized early and proper treatment instituted.

It is unquestionably true that many women who are peculiarly sensitive to pain, and in whom the effects of the pain of a hard labor are severe and lasting, react only slightly or not at all to an operation of more than moderate severity, provided that operation is undertaken before the occurrence of exhaustion. Although it is impossible to predict accurately in every case what patients will react abnormally to the strain of labor, a fair working rule may be established. The patient who does not improve in health during pregnancy and whose condition when approaching her labor is less satisfactory than during the early months of pregnancy, showing that the strain of pregnancy is too great a burden, is seldom or never a fit patient to undergo the strain of an ordinary labor unaided. The patient whose muscular system is flabby and in whom elimination of waste products has been faulty throughout pregnancy must also be placed in the unfavorable class. In addition, the patient whose nervous equilibrium is so unstable that a marked degree of reaction arises from slight discomfort will usually prove a poor subject for labor.

While it is impossible to say with absolute certainty that a patient will not go through labor in a satisfactory way, the chances of an accurate prediction of the end of labor are very great when the

patient has been thoroughly studied. When after due consideration the obstetrician has decided that a certain patient will probably go through labor badly, it is his duty to take such steps as will, in his opinion, do most to insure her safety. According to his judgment the patient may be allowed to go into labor and the effect of labor carefully watched, immediate delivery being undertaken, no matter what stage of labor may have been reached, at the first indication of unfavorable signs. This treatment will be particularly applicable to cases which are on the border line. In other cases he will be absolutely certain that labor will be unsatisfactory, and in these cases the indication must be to end the pregnancy at a set date by operative procedure. The operation in these cases must be chosen without losing sight of the patient's future interests, and the operation to be performed must be the one which is least liable to result in injurious effects to the future health of the patient.

Until very recently the choice of operation in the absence of definite pelvic contraction, or at least of a faulty relation between the child and the mother's pelvis, was limited to delivery by forceps or version, according to the indications, but the point must not be lost sight of that the health of many a woman has been temporarily or permanently sacrificed on account of injuries to the pelvic organs which occurred during a normal or operative delivery. Therefore, the study of the individual patient on whom operation before labor begins is considered advisable, must include the estimation of the probable damage which will result from delivery through the natural passages.

Given a young woman whose muscles are not rigid, in whom there exists a normal relation between the child and the pelvis, delivery from below is unlikely to be attended with serious consequences, but in the case of an elderly primipara with rigid soft parts the dangers of a pelvic delivery leaving serious after-effects are materially increased; and in these cases there is no question that abdominal delivery will probably give best results.

The present status of the early Cesarean section is that the operation, performed before the beginning of labor under proper conditions and by a competent operator, is practically without danger to life or to health, and there can be no doubt that in many cases it offers distinctly the best chance for a proper recovery. The advocacy of an elective Cesarean section for patients who have no pelvic obstruction will undoubtedly come as a shock to many members of the profession, who have heretofore considered obstetrics as a science to be conducted by rule of thumb according to traditions laid down by past generations. Let any man, however, who has had an extensive practice among the women of the overcivilized class, honestly consider patients he has seen, whose health has been wrecked by so-called conservatism, and who subsequently required a more or less serious operation to restore them to even a moderate degree of health, and ask himself the question whether these patients would not have been

better off if some method had been employed at the time of delivery which, though seemingly rash, would have prevented not only the nervous exhaustion of prolonged labor, but the damage to the pelvic organs which resulted from one of the so-called conservative operations.

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## THE RELATIVE SEVERITY OF THE DIFFERENT FORMS OF THE TOXEMIA OF PREGNANCY AND ITS BEARING UPON THE TREATMENT.<sup>1</sup>

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AN attempt to classify the different forms of toxemia occurring during pregnancy, based upon the organ most seriously involved, includes a dissertation upon some points in etiology that are extremely indefinite. We can only correlate the evident manifestations of disease to reason out a cause, primary or secondary, for the relative severity of the form presented. A study of this relative severity based upon classified causes, even though secondary, has some bearing upon the question of the termination of pregnancy.

Toxemia may be due to some perversion of metabolism in the intestines, in the parathyroids or thyroids, in the foetal organism, in the placenta, in the kidneys, or in the liver, and still such a manifestation of disturbed metabolism may be only the showing out of the weakest point in that person and be caused primarily by a single form of toxemia produced by some perverted metabolism in syncytial tissue. The point I wish to make, however, is this: be this as it may, certain it is that the changes in the liver, for example, add greatly to the unfavorable prognosis; and when such toxemia proceeds so far as to involve the liver, or when the person presents this as her weak point early in the toxemia, a much more serious grade of toxemia is present.

It is perhaps a step forward if we can adduce evidence to prove that some one organ is the principal cause or is more profoundly disturbed in any case of toxemia, and if by such aid in classification we can get some help as to alleviation or as to when to terminate the pregnancy, if necessary.

Basing our ideas upon this, we have heretofore classified toxemias, naming them in the order of their severity or danger to life, from the least to the greatest, as those due to: (1) Intestinal disturbances, (2) thyroid gland disturbances, (3) parathyroid gland disturbances,

<sup>1</sup> Read at a meeting of the Philadelphia Obstetrical Society, February 6, 1908.

(4) foetal disturbances, (5) placental disturbances, (6) kidney disturbances, (7) liver disturbances, and (8) bearing in mind the possibility that in rare instances any one of the other glandular structures may be the principal organ at fault.

The simplest form of toxemia, that due to intestinal disturbances is so common that fully 50 per cent. of pregnant women suffer from it in some form. It is also true that disturbances of digestion are one of the primary and usual manifestations of many other toxemias. There are two usual forms of primary intestinal toxemia, that due to constipation and absorption of poisons, and that due to indigestion and generation of poisons also absorbed. The following is an example:

CASE I.—A patient was brought to a maternity in an unconscious condition having had several convulsions. She was a multipara, pregnant about thirty-eight or thirty-nine weeks. She had not had a bowel movement for some days; the exact time was not known. Lavage of the stomach with the use of active cathartics and lavage of the bowel by the rectum resulted in some five hours in free liquid catharsis, during which time she had one convulsion. The relief of the bowels relieved the pulse tension and the patient improved, had no more convulsions, and proceeded some six hours later to deliver herself normally. When rational she acknowledged not having had a bowel movement for five days.

From this advanced stage we may proceed backward to all grades of such toxemia, to the mildest form of headache and nausea because of lack of free evacuations. There is a peculiar tendency of the cells of the intestinal mucosa during pregnancy to favor constipation.

Any preëxisting defect, such as recent typhoid fever, acute or chronic enteritis, etc., is usually cause for disturbed digestion and assimilation of food, principally the proteid or purin principles. There will remain some difficulty in differentiating this primary form from such as are symptomatic of disturbances elsewhere.

The promotion of healthy movements of the bowels, with lavage, will clear up the toxemia and the diagnosis. I have never been fully convinced that this constipation or other glandular disturbances in the intestines may not be a primary causal factor in all toxemias, because if allowed to continue it produces an absorption toxemia that starts a more serious defect in the liver, kidneys, etc., and which if early corrected avoids these severe forms.

There seems to be an increased demand thrown upon the thyroid in all normal pregnancies; any deviation from this results in a toxemia of varying intensity and somewhat startling manifestations. Two short *resumes* may illustrate:

CASE II.—A primipara, illegitimately pregnant, presented this peculiar menstrual history: since the beginning of the function she had had a scanty flow, but perhaps a few times each year. She is twenty-three years of age. A vicarious flow from the nostrils and the

bowels has been present at times. As pregnancy advanced a profound anemia became apparent; there was some bleeding even during pregnancy from the bowels, and on one or two occasions she vomited blood; the quantities shown me were not large. The urine gave no evidence of nephritis; the total quantity is not known. The toxemia progressed and her anorexia and sleeplessness became more marked. The thyroid showed some enlargement. The usual medication produced no result. Five grains, four times a day of thyroid extract produced a marked amelioration of symptoms and an improvement in tone in digestion, and in quantity of urine. She delivered herself at term of a toxemic, wizened child, with no bleeding.

CASE III.—A multipara, who had had some slight cedema, but no signs of kidney breakdown, became evidently toxic, which may have been due to a number of causes: lack of personal and bowel hygiene and indiscriminate eating of proteids and poor elimination. Her thyroid is much larger than is usual to find during pregnancy; she avers that the gland became large during her first pregnancy and never fully returned to normal, and enlarged markedly during two succeeding pregnancies. Her headache became excessive, exposure induced an infection, and with increased cedema and symptoms of impending convulsions with anuria, she went into labor and delivered herself of a male child. The specimen of urine examined showed abundant albumin and casts, evidence of fresh kidney breakdown. For the anuria and headache I gave her before delivery a capsule containing 1 grain of thyroid extract,  $\frac{1}{2}$  grain of caffeine citrate,  $\frac{1}{10}$  grain of calomel, to start the stimulation of excretion and elimination. She had scarcely taken three of these capsules, at two hour intervals, when I was sent for hurriedly. The thyroid, which had been enlarged slightly above normal, was tense and both lobes were as large as a cystic goitre; such it resembled, pulsating somewhat from tension of the vessels; so tense and rapidly had it developed that the patient was compelled to sit up gasping for breath; the headache also was intense. I stopped the capsule and used an ice-bag to the throat with good effect, although forty-eight hours elapsed before the tumor subsided, and eventually the bowels and kidneys acted. The patient made a gradual recovery, with persisting nephritis.

The amelioration of symptoms in Case II, due to the use of the thyroid extract, showed a toxemia due to lack of thyroid secretion; that of Case III was a toxemia due to a disturbed metabolism brought on by exposure, infection, and evident increase of thyroid secretion. While the kidneys were in the main at fault some months later this patient still showed signs of uremic intoxication, while today she is practically well.

A somewhat rare form of toxemia, so far as our present knowledge goes, hard to diagnosticate and correct, is that produced by disease, or shall I say disturbance, in the foetus. This is well illustrated in the

following patient, whose history record at the maternity has been lost, but my own individual notes are sufficient:

CASE IV.—Mrs. R. came under my care in the maternity ward of the Presbyterian Hospital in labor. During the preceding six weeks she had a temperature ranging from 102° to 103°. Examinations had been made for many infections, typhoid and paratyphoid fever, tuberculosis, and malaria, all to no avail. Finally, because of some alternating character of the temperature, she was placed on large doses of quinine, with the result that labor was brought on. She delivered herself easily of a child at about thirty to thirty-two weeks gestation. The child lived some six hours. The placenta was destroyed before I reached the ward the next day. The patient's temperature fell to normal after delivery. While this is the usual course in any infection during pregnancy, in this instance it stayed at normal and the patient was immediately relieved, and made a quick and easy recovery. We were unable to obtain an autopsy on the child.

This case seems to me to illustrate a form of toxemia due to some vice in the foetus, classifiable possibly among the forms produced by absorption from a dead foetus in the womb or from a syphilitic child. It is rarely an overwhelming toxemia, and usually corrects itself by the expulsion of the offending body.

That form of toxemia due to placental or syncytial tissue may be of a severe type, may even be the primal cause of all toxemias, and when partaking of some forms becomes a malignant invasion of the syncytial cells, added to a toxemia from perversion of metabolism.

Primary kidney toxemias are not as frequent as primary liver toxemias, but late in any toxemia a secondary kidney lesion of greater or less severity is the rule. I purpose now to point out some cardinal points of difference between these two forms, and to discuss their diagnosis as bearing upon a conservative termination of the pregnancy.

A pregnant patient with a preëxisting kidney lesion or a bad aortic or mitral stenosis gives cause for a grave anxiety. She may not be able to go to term, but this is overbalanced by the fact that we have visible and palpable means of keeping watch upon her condition. Rarely should a nephritic or cardiac patient pure and simple proceed to convulsions, since any careful man has evidence forced upon him long before the storm breaks that his patient is doing badly.

There is this to be said about a pure uncomplicated case of nephritic toxemia. The evidence appears early in toxemia in the urine, and if repeated careful estimations show increase coincident with active treatment, the course of action is clear, ample time is given, and the patient reacts more quickly, the danger to the life of the mother is less, and the hope of an ultimate cure is greater in this form than in the latter form, which is, I believe, more common, more insidious,

and, allowing personal equation, claims a greater number of patients than any other form.

Four interesting cases came under my observation during the last year at the Presbyterian Hospital Maternity. Three of these were toxemias without eclampsia, the fourth had some few convulsions.

CASE V.—Mrs. W., a primipara, was admitted June 1, 1907. She was a short, flabby, reddish haired, white woman, with cedema of the face, feet, vulva, etc. She had no convulsions. The last menses occurred December 24, 1906. She had felt life until the day of admission. There was a systolic murmur at the aortic and the mitral area. The bowels opened freely on the day of admission and each previous day. On June 2, examination of the urine revealed 1016 specific gravity, neutral reaction, a heavy cloud of albumin, and many granular and epithelial casts. She was placed immediately upon active eliminative treatment. In spite of steam baths, packs, and purging, the cedema of the vulva increased and the albumin in the urine increased, ranging to four per mille by the Esbach method.

On June 11 we induced delivery by avulsing the cervix, packing with gauze, removing it in twenty-four hours, and inserting a Voorhees bag for twelve hours, and then etherization and manual dilatation. A dead foetus, possibly six months, was removed; the placenta was removed manually. The delivery was slow, but there were no convulsions. There was slight fever and odor to the discharge, and some fever from disorder of the breasts, which readily subsided.

On June 17 the urine had a specific gravity of 1010, was alkaline and contained albumin, four and one-fourth per mille by the Esbach method, and a few hyaline and granular casts. On June 23 the urine had a specific gravity of 1012, and contained albumin, four per mille, and many hyaline casts.

This patient has been kept under constant supervision. On December 15, 1907, her urine still showed a trace of albumin, but no casts. A high grade of anemia developed, but gradually improved.

This is undoubtedly a nephritic case. We did not allow the toxemia to proceed to any interference with the function of the liver. The evidence of toxemia was so evident that her physician sent her in for delivery, and after trying eliminative treatment we were convinced that it would be impossible to carry the child to viability.

CASE VI.—Mrs. M. D., a multipara, was admitted April 15. She had had eclampsia four times, and was now pregnant seven to eight months, and evidently markedly toxic. She had not notified her physician of the pregnancy until sending for him, with excessive headache, substernal pain, and high grade anemia. Because of previous experience her physician suggested immediate delivery. Since there had been no convulsions and eliminative treatment had not been tried, and as we had not seen a urine report, we felt justified in trying elimination and waiting until morning, in the presence of a

rigid multiparous cervix. By the morning the patient was blind, and the toxemia had made rapid inroads in her hemoglobin. The urine report showed a specific gravity of 1020, acid reaction, a cloud of albumin, hyaline and pale granular casts, and blood. We immediately started delivery by metal avulsion and inserting a small bag. Securing no result in six hours, we gave chloroform, and, using Newell's dilators, delivered by "accouchement forcé." The operation required thirty to thirty-five minutes; but little chloroform was used. The uterus was firmly packed with gauze and salt solution was given. Nine hours after operation the patient died, her skin turning rapidly to a golden yellow. No autopsy was permitted, but the picture was that of a rapid blood disintegration or acute yellow atrophy of the liver.

This patient presented the liver type of acute toxemia. She may have had a preëxisting nephritis, but her death was caused by the liver breakdown. One may reserve a neutral opinion that this was due to the chloroform. I shall not in such cases again use chloroform, but from the rapid demise I feel it may only have hastened, not caused death. There were no convulsions.

CASE VII.—Mrs. S., a primipara, five to six months pregnant, was admitted having had a few convulsions. She was conscious, but had had the usual prodromal symptoms, headache, persisting nervous insomnia, etc.; the bowels had been kept open with no avail. No urine examination had been made, there had been no decrease of the proteid intake. The catheter revealed 3 ounces of pure blood. She did not respond to steam bath, but promptly had another convulsion. Ether was given, the cervix opened with the hand, and a living six months child extracted. The patient was then bled and transfused. She did not have another convulsion. During the first twenty-four hours we secured by catheter 9 ounces of pure blood; then the kidneys responded somewhat to treatment, and we secured 52 ounces of moderately clear urine. From that time on she made a rapid recovery. Now her urine has a specific gravity of 1016, and contains no albumin and no casts.

These reports of startling emergency cases serve to enforce the conclusions in regard to careful urine examinations in such cases. Without exception the hepatic disturbance, be it primary or secondary, is the leading factor in the mortality.

In a nephritic patient the toxemia may, if allowed to proceed, involve the liver. Such added tissue involvement is the most serious factor in that patient. Primary liver toxemia is a most insidious disease so far as symptomatology goes; only late in the toxemia do we find a nephritis. If this be in any measure true, it is of the utmost importance to be able early to classify cases as liver toxemias, to watch them closely, and to know at what point in the course of the toxemia irreparable harm is being done.

The diagnosis of the liver condition may be arrived at by interro-



gating the patient and excluding all other sources as a cause for the symptoms; then examining the excretions. If one gets a basis or starting point, repeated careful examinations will certainly show some changes if for the worse; the condition of the patient, together with these readings, is sufficient evidence for definite treatment. Repeated studies have demonstrated that to aid the diagnosis it is necessary to study the urine, not only for albumin and casts, but also to estimate the total daily output of nitrogen, to divide this nitrogen into its sources—urea nitrogen, ammonia nitrogen, purin nitrogen, or uric acid creatinin nitrogen, and amino-acid nitrogen.

Repeated examination of such cases, of which the foregoing are but final pictures, lead to the conclusion that in the most serious forms of toxemia there is to be noted perhaps only a decrease in the daily quantity of urine, then perhaps an added decrease in the total daily output of nitrogen in the urine, that is, if the patient is on a milk diet. Then, with persistence of the toxemia changes in the ratio of the different nitrogens occur, usually a decrease of urea nitrogen and an increase of ammonia nitrogen or of amino-acid nitrogen, or of both. Any decided increase or persisting increase in the ammonia nitrogen or in the rest nitrogen is an indication of serious, irreparable changes going on in the liver, and the presence of such low nitrogen output and persisting increase of these nitrogens at the expense of urea should lead to the induction of labor, irrespective of albumin and casts.

We must not be blind, however, to the fact that there is a form of grave nephritis which may produce death, and which shows upon urinary examination albumin and casts and a normal or nearly normal ratio of the nitrogens. The toxemia producing pernicious nausea and vomiting is undoubtedly an overwhelming one and may be studied by the same methods.

The form of toxemia producing chorea, melancholia, mania, etc., is also evidenced by changes in the nitrogen output. I have had the opportunity to study but a very few cases of these two forms, and cannot form definite conclusions as yet. I may conclude as follows:

Considerable aid as to the kind of and advance of the toxemia may be gained by careful and repeated urinary examinations; but such examinations take but the place of all laboratory reports. Any decision as to the use of the therapeutic measure, the termination of the pregnancy, must be based upon the condition of the individual patient, and while we at no time should be eager to do this, yet should the laboratory finding and the symptoms suggest liver involvement it must always be kept before our minds as a possible necessity.

## THE OCCURRENCE AND SIGNIFICANCE OF NEGATIVE RESULTS IN BLOOD-CULTURE STUDIES.<sup>1</sup>

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In practically all of the blood-culture studies which have been published attention has been drawn mainly to the positive findings and their significance. As the result of a study of over 1500 cases of fever by means of cultures made from the blood, we have been impressed with the importance of directing attention to the significance of negative results in cases in which the question of the presence of a bacteremia has been brought up. It is my purpose to present to you the main facts which have been brought out by our studies.<sup>2</sup> A consideration of all the data at our disposal would not be practicable, because we should become lost in a mass of detail and because a number of points are still under consideration.

In discussing this subject, it will be necessary to speak largely on a number of subjects which belong more or less to the domain of surgery and the surgical specialties. But the internist is so often called upon to help elucidate the cause of febrile complications of surgical diseases or the cause of a fever unduly continued after the performance of an operation, that I have considered it advisable to present the subject here.

### *I. Under what conditions do we find blood cultures (properly made) negative in cases in which the existence of a general bacterial infection is suspected?*

1. The case may not be one of infection by one of the bacteria easily cultivated by our present methods.<sup>3</sup> It may be a case of tuberculosis, actinomycosis, or syphilis; it may be due to an infection by protozoa; it may be due to parasites of any kind which have not yet been isolated. It may be a case of newgrowth with fever, or a case of disease of the hematopoietic organs (Hodgkin's disease, pseudo-leukemia, etc.). It is particularly when these last-named conditions are confined to the abdominal cavity and give no characteristic local findings that the diagnosis of a general infection is often seriously entertained.

<sup>1</sup> Read at a meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1908.

<sup>2</sup> I have discussed this question briefly on another occasion (Johns Hopkins Bulletin, July, 1906).

<sup>3</sup> We include here the following organisms: the typhoid bacillus, paracolon bacillus, colon bacillus, meningococcus, Bacillus proteus, Bacillus mucosus capsulatus, gonococcus, Bacillus pyocyaneus, glanders bacillus, anthrax bacillus, streptococcus, pneumococcus, Streptococcus mucosus, staphylococci, influenza bacillus, and the attenuated cocci found in certain cases of endocarditis.

2. The case may be one of infection by one or more of the ordinary bacteria, but they may not be present in the blood at the time the blood culture is made. We must discuss here the so-called specific fevers, on the one hand, and the local infections due to the pyogenic organisms, on the other.

(a) So many studies of the bacteriology of the blood in the specific fevers have appeared in recent years that there is little new to be added. In pneumonia, as is known, different authors have found organisms present in varying percentages of the cases. While it is probable that the blood contains cocci at some time in every case, we cannot be sure (except, perhaps, in very severe cases) of finding the cocci in a given case at the time when we make our examination.

In typhoid fever the bacilli seem to be present in every case until within a few days before the temperature discontinues being constant. After that time the chances of finding the bacilli become less and less.<sup>4</sup> In paratyphoid fever the same rule probably holds good. But there are not enough cases of this disease studied as yet.

In cerebrospinal fever the organisms quite frequently are not found in the blood. Elser found them present in 25 per cent. of the cases. According to our experience, they may be present early in the severer cases, and are present in cases which have fever (and arthritic and cutaneous phenomena) before the meningitis develops. (Cases have been reported in which no meningitis developed.)

In influenza we have had negative results, but our studies have not been extensive. There are not many indubitable positive findings in the literature. In rheumatism and rheumatic endocarditis we have found no bacteria in the blood. The frequency of bacteremia in glanders we do not yet know. It would appear that the bacteremia occurs frequently in the acute type.

I might interpolate here that in tuberculosis of the lungs neither in early nor in advanced cases have we encountered any examples of invasion of the blood by the pyogenic bacteria.

(b) In discussing the cases of infections due to the so-called pyogenic bacteria—and these form the basis of the more valuable of our studies—I shall group with the streptococci and staphylococci the pneumococcus,<sup>5</sup> *Bacterium coli*, *Bacillus proteus*, *Bacillus mucosus capsulatus*, and gonococcus.<sup>6</sup> While local infections and bacteremias due to the last-named organisms are not very frequent, a study of our cases indicates that the same rules regarding general invasions apply to them as to infections by streptococci and staphylococci.

<sup>4</sup> In several cases corresponding to the so-called post-typhoidal sepsis we have not found any bacteria in the blood.

<sup>5</sup> In including the pneumococcus here, I have reference to those cases only in which pneumonia is not the primary lesion.

<sup>6</sup> The bacillus pyocyaneus and anthrax bacillus are so infrequently found that I shall omit them from consideration here.

While we cannot deny that in every local infection at some time or other bacteria are present in the blood, our studies show that there is a number of reasons why we do not find bacteria in the blood in a given case at a given time.

The bacteria may not be demonstrable at any time in a given case. Often they are present early in the course of the infection and disappear later with or without secondary foci being established. These foci may be established some days after the bacteria are no longer found in the blood current. When the valves of the heart become infected, the bacteria are found in the blood. An exception to this statement will be noted in the second section of the paper.

The organisms may be present in the blood only until the local focus has been properly operated upon. It is often remarkable to see how rapidly a marked bacteremia will disappear after ligation of the jugular vein in a case of sinus thrombosis or after an operation for osteomyelitis. In a case of sinus thrombosis recently studied, two hundred colonies of *Streptococcus mucosus* were found in each cubic centimeter of blood. Two days after ligation of the jugular vein the blood contained no bacteria. In a case of osteomyelitis of the humerus there were found five hundred colonies of *Staphylococcus aureus* to the cubic centimeter of blood. Three days after operation the blood was sterile.

At times the bacteria will invade the blood current for a short time during the course of the disease. This may at times be due to surgical intervention in a case in which bacteria were not previously demonstrable.

In some cases we must assume that metastatic foci are set up by the passage of a bit of infected thrombus through the blood (so-called "infection by transport"). At times this happens even when there is no macroscopic evidence of thrombus formation. In such cases bacteria may not be demonstrable in the blood. When a secondary focus has been established in this fashion and the peripheral venous circulation is not part of the pathway of the infected material, it is still easier to understand how metastatic foci can be developed without bacteria being found by means of blood cultures. Such a condition is seen, for example, when a brain abscess is caused by the lodgement of a bit of thrombus from a pulmonary vein, in a case of empyema.

In connection with some forms of local infections, particularly when they are extensive, bacteremia is quite frequent, subject to the conditions I have described. In cases of osteomyelitis, in particular, systemic invasions are frequent. In a number of others it is surprising to find that, notwithstanding the fact that the lesions are often extensive and severe, bacteremia is not often found. I shall cite some of these conditions:

1. Secondary Parotitis. In the rare instances in which the parotitis is a true metastatic infection bacteria may be found in the

blood. But in the form which complicates operations and abdominal or other disease, and which is supposed to be a mouth infection, we have not found bacteria invading the blood from the inflamed gland.

2. Erysipelas. In only one case (nasal erysipelas) did we find a bacteremia.

3. In cases of mammary abscess, no matter how extensive, we did not meet with any invasions of the blood.

4. Empyema does not usually cause a bacteremia.

5. In osteomyelitis of the inferior maxilla we have not seen a bacteremia, even when the condition was complicated by thrombosis of the cavernous sinuses.

6. In cases of liver abscess we have seen a bacteremia only when they were cholangitic in origin.

7. In cholecystitis, we have been able to demonstrate a bacteremia only when cholangitis was present. This subject requires further study.

8. Appendicitis. We have studied 60 cases of various types. In none were bacteria present in the blood. In one case which came to autopsy there was found an acute endocarditis of a type in which we always find bacteria in the blood. No culture had been made during life.<sup>7</sup>

9. In a study of cases of peritonitis secondary to intestinal disease (appendicitis, necrosis of the intestine due to various causes, etc.), we were surprised to find no positive blood cultures.

10. In the pyelitis of pregnancy it is the exception to find bacteria in the blood.

11. In cases of extensive infective thromboses, purulent or non-purulent, bacteria may be absent from the blood. In sinus thrombosis most of the cases show bacteremia early, but some do not later in the course of the disease. Some cases of thrombosis of the pelvic veins and inferior cava following infections of the female genitals are unaccompanied by a bacteremia throughout, even though there may be metastatic abscesses of the lungs present.

We have studied fifteen cases of suppurative pyelephlebitis, most of which were accompanied by liver abscesses; in only one was a bacteremia demonstrable (pneumococcus). But in this case the infection of the vein was due to a cholangitis (due to calculous cholecystitis), and this condition may have been the starting point of the bacteremia. In the cases of pyelephlebitis with very numerous liver abscesses bacteria must at times be free in the portal vein. To this and similar conditions I have applied the terms "cryptic bacteremia" and "partial bacteremia." We could also speak of a "portal bacteremia."

<sup>7</sup> Sheitlis has reported a case of streptococcemia in appendicitis (Medical Record, November 2, 1907).

## II. *Of what value are negative results obtained in the course of examinations of the blood for bacteria?*

The data which I have given, when studied in connection with individual cases, will yield many facts of diagnostic and therapeutic value. I shall attempt to emphasize some of the more important conclusions that we have been able to draw. It is hardly necessary to direct attention again to the necessity of controlling the bacteriological and clinical studies by means of each other.

1. In the grouping of certain cases for study, negative blood-cultures are of value. For example, cases of chorea without bacteremia<sup>a</sup> should be classed separately. The same holds true of such conditions as the erythema group, acute toxic icterus, and the purpuric diseases. When we obtain from the blood of such cases bacteria such as I have listed above, we must consider the chorea, erythema, or purpura, as the case may be, a clinical picture due to the toxins produced by the bacteria found. The cases with negative cultures should be kept in a separate group for study. Later investigations may show that even this group is not due to a single etiological factor.

2. In a case of supposed typhoid fever, if the blood-cultures have been negative and the temperature remains constantly high for three or four days longer, it is important to consider the possibility that one is dealing with another condition, and not simply view the case as one of typhoid fever in which the bacilli have not been found. In a case which I observed last summer, with enlarged spleen, atypical roseola, constant temperature, and abdominal symptoms, two blood cultures were negative. The temperature remained constant, about 104° to 106°; the Widal reaction was absent. The case proved to be one of general miliary tuberculosis. The abdominal symptoms, which for a time led us to fear a perforation, were due to recent peritonitis over the spleen, liver, and a coil of intestine in the right iliac fossa (due to tuberculosis of these viscera). I felt that we could have earlier suspected the correct diagnosis (we suspected it only on the day before death) had we laid greater stress on the negative cultures with a continuance of a constantly high temperature.

3. A negative blood culture may at times be good corroborative evidence of the diagnosis of acute articular rheumatism. In some cases of general infection by the ordinary pyogenic cocci the clinical picture may resemble rheumatism (the fluid in the joints may or may not later become purulent). We have seen this particularly in cases of infection of otitic origin. In some cases of supposed rheumatism we have, by finding attenuated cocci in the blood, such as are found only in cases of subacute or chronic infection of the

<sup>a</sup> I exclude all agonal and terminal invasions in the remarks that follow.

heart valves, been able to draw attention to the real seat of disease in the patient.<sup>9</sup>

4. When a patient has a local infection with very severe constitutional disturbances, it is often of prognostic value to know that there are no, or not many, bacteria in the blood.

Last fall I took care of a man who suffered from an inguinal adenitis and cellulitis with a constitutional disturbance of such severity that we were very suspicious of a severe general infection. The primary focus was opened up, some pus evacuated. The blood culture was found negative, a fact which made the situation much less tense. The profound constitutional disturbance disappeared rapidly, the patient making a good recovery. No metastatic foci developed.

5. If a patient has a local infection that has been operated upon, and general symptoms persist, a negative blood culture shows that there is no systemic invasion. Either the local trouble has not been cleared up or there exist metastatic infections or an intercurrent disease. If the local infection is so situated that it can be properly explored, and if such examination does not show sufficient trouble to account for the symptoms, metastatic foci or intercurrent conditions are surely present.

We have seen many instances in which this view point was of value. In a case of cholecystitis the symptoms continued after the gall-bladder was drained. A general infection was believed to be present by the surgeon, but the blood culture was negative. A subphrenic abscess was later found and opened. The symptoms continued, and a general infection was again assumed to be present, but a negative blood culture again showed that a general infection could be excluded. Later, an interlobar empyema was found. Often the report of a negative blood culture has thrown out a diagnosis of general infection, and later a tuberculosis of the lungs or some other part of the body has been found as a cause of the persistence of symptoms after a pus focus had been properly attended to. I could cite many other examples.

A patient should not be considered as having a general infection unless bacteria are demonstrated in the blood. Much harm may otherwise be done. And I may state here again that a small number of bacteria cannot by themselves be held accountable for marked constitutional symptoms.

6. If a patient has had a local infection and bacteremia, and the bacteremia disappears after operation, this constitutes a certain amount of evidence that the local infection is under control.

7. If a patient has, or has recently had, a local infection, a diagnosis of infection of the valves of the heart (so-called "malignant" or

<sup>9</sup> Cases in this group quite often present arthritic phenomena. As a rule, however, the joint changes are not of a markedly acute type.

"ulcerative endocarditis") cannot be made if the blood cultures are negative. In cases in which the heart valves were infected from local lesions we have found bacteria in the blood in every case except one. That was a case, in the service of Dr. Manges, of gonorrheal abscess of the mitral valve. Originally the organisms must have passed through the blood to have infected the valve. But the negative results of our cultures were easily explained by the fact that the only lesion on the valve was a closed sac containing pus full of gonococci. Cultures at an earlier date might have been positive. Fortunately the diagnosis was not difficult clinically. As it is well known that the gonococcus is not as easy to cultivate as many other organisms, one must be more guarded in giving his opinion in cases of infection by this organism.

We have had only one case in which the bacteria were present in one culture and not in an earlier one, although the endocarditis was clinically present when the earlier culture was made. At the time at which the case was studied (six years ago) our methods were not as good as they are now. Nevertheless, we would recommend the making of two cultures in all doubtful cases.

The point which I raise in this section is important, because when a diagnosis of "malignant endocarditis" is once made, less or no attention is apt to be paid toward clearing up a primary focus or secondary foci. In a case of osteomyelitis of the pubes which had been thoroughly treated, a consulting surgeon stated that the case would be fatal because "malignant endocarditis" had supervened. There was present enough clinically to suggest such a diagnosis. On the basis of a negative blood culture I stated that it was not wise to diagnosticate a valvular infection, and that some other cause should be searched for. There was found an osteomyelitis of the upper end of the left femur. This was operated upon and the patient recovered, the constitutional disturbance disappearing promptly.

8. In chronic endocarditis with fever, negative blood-cultures are of value in excluding recent bacterial infections of the valves. In some of the cases the fever curve and the other clinical phenomena are almost identical with those seen in some cases of so-called "ulcerative endocarditis." It is unnecessary to discuss here the various conditions that may be the cause of more or less prolonged fever in cases of chronic endocarditis. It is particularly in the cases in which bits of thrombotic material or bits of lime from a calcareous valve are being thrown into the circulation, and in which petechiæ are present that we find the resemblance to certain cases of recent bacterial infection of the valves.

In a patient with chronic endocarditis, who is suffering from a local infection anywhere in the body, a negative blood culture may be the only means of excluding an infection of the heart valve. In such a patient a negative blood culture at the height of the infection is



very reassuring, for there is often present the fear of the development of an acute endocardial lesion.<sup>10</sup>

9. Negative blood cultures are at times of service in the diagnosis of infective thromboses of veins, and especially in the differential diagnosis between such conditions and acute endocardial lesions.

In cases of postpartum infection, negative blood cultures with the co-existence of repeated attacks of chills and fever with leukocytosis, even if there are only slight or no local phenomena, point to thromboses of veins in the pelvis (of course, other causes, such as a pyelitis or malaria must be excluded). When the question of ligation of the veins comes up it may be important to exclude the diagnosis of acute endocarditis.

Occasionally negative blood cultures will help us in establishing the diagnosis of pyelephlebitis. When it is known that a patient has had a local infection in the portal territory (for instance, an appendicitis, or a gangrenous hemorrhoid), it is natural to think of a suppurative pyelephlebitis if there develop repeated seizures of chills and fever and a high leukocyte count.

But there occur cases of infective thromboses (purulent or non-purulent) in the portal system in which there is no clinical evidence of a primary intra-abdominal focus, and which are characterized by only vague general or abdominal symptoms, repeated seizures of chills followed by fever of varying height, and a high leukocyte count. Late in the disease the diagnosis may be made simpler by the development of tenderness over the liver, evidences of liver abscesses and some icterus, or a slight or moderate ascites.

It is important in all cases characterized by repeated chills, high fever, and leukocytosis to keep in mind the possibility of thrombotic processes in veins. The veins which are the most important for consideration are the veins of the extremities, the lateral and cavernous sinuses, the pelvic veins, and the veins of the portal system. If the veins of the extremities are affected, the diagnosis is usually evident. If the lateral or cavernous sinuses or the pelvic veins are involved, we have always found a clue in the evidence of the existence of a primary focus. Infections of the cavernous sinuses usually present pronounced local symptoms, by means of which the diagnosis may be made. Infections of the lateral sinus or of the pelvic veins may present no decided local evidence.

By exclusion we must keep in mind in certain cases the possibility of the infection of veins in the portal system.<sup>11</sup> In these

<sup>10</sup> We do not know how often cases may occur in which the valves are infected, and in which the patient recovers and no damage occurs of a type that gives evidence of the implication of the valve at the time of the infection or after recovery. While such a condition is possible, clinically it plays no role.

<sup>11</sup> It is, of course, necessary in such cases to take into consideration the possibility of syphilis, actinomycosis, intra-abdominal growths, disease of the intra-abdominal lymphoid tissues, and obscure forms of tuberculosis. Into the diagnostic questions that arise in this connection I hope to enter on a later occasion.

cases the differential diagnosis sometimes lies between an endocarditis and a pyelephlebitis. But in the cases of endocarditis which we have encountered, in which a picture similar to that found in pyelephlebitis was seen, we have always found bacteria in the blood. So that when the question arises as to whether a patient is suffering from an acute infective endocarditis or a suppurative pyelephlebitis, the absence of bacteria in the blood excludes an endocarditis. It is hardly necessary to add that a positive culture does not exclude a pyelephlebitis because, as I have stated above, it is possible to find bacteria in the blood in the latter disease. The same holds true in connection with the diagnosis of infection of other veins. By following the line of reasoning above given, we have been enabled in several cases to suspect the existence of a suppurative pyelephlebitis in patients in whom there was clinically no clear evidence early in the disease of an intra-abdominal lesion. And in these cases, the postmortem examination confirmed our suspicions.

### **SUGGESTIONS OF THE PUPIL IN GENERAL DISEASE.**

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OF his recent paper on "Ocular Symptoms in Cerebrospinal Meningitis," Ballantyne<sup>1</sup> devotes one-fifth to descriptions of the pupillary symptoms. He states that "abnormalities of the pupils were the most common symptoms. Thus, only 6 out of 69 cases in which the pupils were examined, had no pupillary abnormality." There was inequality of size, mydriasis, miosis, alterations of light reflex, ciliospinal reflex, orbicularis reflex, and in one case total absence of pupil reflexes on the day of death. But he sums up the matter thus: "None of the pupillary phenomena, with the exception of total absence of the reflexes, seems to be of any value as regards diagnosis or prognosis."

An enormous amount has been written about the pupil, some of it contradictory, most of it indefinite, and often what has been positive and definite has been mistaken and misleading. The pupil furnishes no pathognomonic symptoms of general disease. It does not finally settle any doubtful questions of diagnosis. The practitioner who expects it to make the diagnosis for him, or who relies on it to give him positive information of the approaching result, is sure to be disappointed. Swanzy<sup>2</sup> says: "The condition of the pupils, whether normal, contracted, or dilated, is of very slight significance

<sup>1</sup> Brit. Med. Jour., July 27, 1907.

<sup>2</sup> System of Diseases of the Eye, edited by Norris and Oliver, vol. iv, p. 602.

or value in the diagnosis either of the position or of the kind of any intracranial lesion. And yet, slight in value as is the state of the pupils in cerebral cases, there is probably no symptom which receives more regular attention from the clinician in his note-taking."

But to anyone who is on the lookout for clues that he may be able to follow to a positive diagnosis, for suggestions of a possible explanation of the case before him, the pupil is enormously suggestive. The sideroscope, devised to detect the presence of steel within the eye by the perturbations of a delicately poised magnet, is found to work but poorly in the steel-framed buildings and among the industrial electric currents of our large cities. It too easily responds to a multitude of attractions. So the pupil reacts so readily and to so many different influences that in the present state of our knowledge we are quite unable to interpret with certainty its behavior in disease. But it is full of suggestions of profitable lines of investigation for the alert diagnostician in any branch of internal medicine.

Within a few days I saw a man brought into a hospital with consciousness seriously disturbed, following a blow on the right parietal region; but investigation revealed no fracture at that point. The right pupil appeared normal, the left noticeably dilated. There were no other obvious localizing symptoms. Study of the reflexes showed their alteration on the right side, pointing to lesion of the left brain. What the lesion was, just where it was, what would be its outcome, the pupil did not say. But it declared there was a lesion, and that the case was worthy of most painstaking study.

Recently my attention was called to inequality of the pupils in a young man in the Denver County Hospital. It was the left pupil that was dilated. The young man was suffering from pulmonary tuberculosis, and the pulmonary lesion, or at least the first and principal lesion, was situated on the left side. The condition of the pupil was utterly inadequate as a basis for the diagnosis of pulmonary tuberculosis. But how valuable such a suggestion would be in some early cases!

Pernot, who examined 1140 cases of phthisis, found inequality of the pupils present in 6 per cent. of cases in the first stage, in 8 per cent. of those in the second stage, and in 14 per cent. of the patients who had reached the third stage. The altered pupil was on the same side as the chief pulmonary lesion. In the first stage the pupil was dilated. In the second stage it was sometimes dilated and sometimes contracted on the side of the lesion. In the third stage the change was more generally a contraction. Bichelonne<sup>3</sup> examined 69 patients known to be suffering from the first stage of phthisis, or suspected of that disease; and found that 10 presented dilatation of the pupil on the side of the pulmonary lesion.

<sup>3</sup> *Annales d'oculistique*, October, 1905.

The probable explanation of the phenomenon is that the pulmonary disease acts through the sympathetic, an irritative lesion causing contraction of the dilator muscle of the iris. Later in the disease, destruction of the affected fibers produces a paralysis of the dilator, and consequent miosis. Such contraction of the pupil I have repeatedly seen in connection with tubercular disease of the sympathetic glands of the neck. Bicheionne suggests three possible points for the nerve disturbance; (1) Disease of the ganglion; (2) affection of the communicating fibers from the spinal nerves, passing in close contact with the apex of the pleura; and (3) irritation of the branches of the sympathetic, distributed within the lung itself. The last suggestion would serve equally well to explain dilatation of the pupil, which has been observed on the side of the pulmonary lesion in croupous pneumonia; although Sighicelli<sup>4</sup> claims that dilatation of the pupils is always present in pneumonia, and ascribes it to the influence of a pneumococcic toxin.

Signorelli<sup>5</sup> from a study of pupillary reflexes connected with the internal viscera, concluded that inequality of the pupils in general indicates the side of the body on which the lesion is situated. Thus, he considered dilatation of the left pupil an important symptom of disease of the spleen.

Disturbances of the pupil are generally mentioned as one of the symptoms of disease affecting the arch of the aorta. The explanation was that these disturbances are due to the involvement of the cervical sympathetic in the local disease. Irritative conditions caused dilatation, and destructive lesions, miosis. This explanation was unchallenged for many years.

However, Babinski<sup>6</sup> pointed out that the clinical facts frequently did not fit the explanation; and he suggested that the real relation of the pupillary symptoms to aortic disease was that they had a common cause—syphilis. Chaillous<sup>7</sup> reported two cases of aortic dilatation supporting Babinski's view. In one the condition of the pupil was dependent on complete ophthalmoplegia interna. In the other case there was complete loss of the light reflex, not simple inequality of the pupils. Vaquez<sup>8</sup> reported two cases of syphilitic disease confined to the valves of the aorta, in which there was loss of the light reflex, and inequality of the pupils. Rodiet<sup>9</sup> upholds Babinski's view; and Braillon<sup>10</sup> reports cases of mitral disease in support of it.

This question regarding aortic disease brings up the general subject of the pupil in syphilis. It ought to be recognized that all abnormalities of the pupil not due to temporary causes are very suggestive of syphilis. In 1900 Harris<sup>11</sup> advanced and strongly

<sup>4</sup> *Gaz. med. Lomb.*, 1900.

<sup>5</sup> *Proc. soc. des hôp.*, November, 1901.

<sup>6</sup> *Recueil d'ophtalmologie*, May, 1902.

<sup>10</sup> *Gaz. des hôp.*, June 21, 1906.

<sup>7</sup> *Riforma med.*, xxii, No. 36.

<sup>8</sup> *Annales d'oculistique*, July, 1902.

<sup>9</sup> *Ibid.*, November, 1906.

<sup>11</sup> *Brit. Med. Jour.*, September 29.

supported the view that the loss of the light reflex, with preservation of other pupil movements (the Argyll-Robertson symptom), was not a symptom of locomotor ataxia, but a symptom of syphilis. Lesynsky<sup>12</sup> had before that suggested that unilateral reflex iridoplegia was generally of syphilitic origin. Dufour<sup>13</sup> has never seen this symptom except in syphilis. Nageotte<sup>14</sup> accepts this view of the symptom.

I have seen three patients—a man aged thirty-one, a woman aged thirty-six, and a woman aged twenty-eight years—who presented complete loss of the light reflex without any other symptom of locomotor ataxia. These patients were all of them first seen more than six years ago. One of them continued under observation for over three years. So far as I know, no symptoms of locomotor ataxia subsequently developed. The first two gave the history of syphilis; the third was strongly suspected of syphilis, although her history pointed to the immediate causation of this trouble by an attack of influenza.

Sulzer<sup>15</sup> has called attention to disturbance of the pupil reactions entirely apart from hyperemia or inflammation of the iris, as a transient, early, secondary symptom of syphilis. Among 53 cases, he mentioned such symptoms in fourteen.

With regard to abnormalities of the pupil, however, we should bear in mind that at this altitude (Denver, 5280 feet), and to a greater extent at still higher altitudes, cases of partial ophthalmoplegia interna occur more frequently than elsewhere. Some of these cases are apparently not connected with syphilis. The dilatation of the pupil is always in my experience accompanied by weakness of accommodation, and one eye is always more affected than the other. I have seen a case of this kind recover completely, after several weeks' sojourn at a low altitude without other treatment. Such patients have always been benefited by remaining some time at a low altitude; in general health as well as in the ocular paralysis. The need of temporary removal to a lower altitude may be taken as one of the suggestions of this condition of the pupil.

<sup>12</sup> New York Med. Jour., August 6, 1898.

<sup>13</sup> Gaz. hebdomadaire de médecine et de chirurgie, June 19, 1902.

<sup>14</sup> La presse médicale, December 4, 1901.

<sup>15</sup> Ann. de dermatologie, March, 1901.

# RAYNAUD'S DISEASE, ERYTHROMELALGIA, AND THE ALLIED CONDITIONS IN THEIR RELATION TO VASCULAR DISEASE OF THE EXTREMITIES.<sup>1</sup>

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At a meeting of the Association of American Physicians, in 1901, I called attention to the intimate relation existing between certain vasomotor neuroses and trophoneuroses, and vascular disease of the extremities. At that time it seemed to me to be important to prove that Raynaud's disease and erythromelalgia are not independent morbid entities, but symptom groups, pure and simple, that might in rare instances be associated with central nervous disease, but are far more often the expression of disease of the peripheral bloodvessels. It was conceded then, as it is conceded now, that these vasomotor and trophic affections may be due to some occult (say trophic) influence, but in the end it was the interference with the peripheral blood supply that was the direct cause of the clinical symptoms. The majority of writers had recognized that Raynaud's disease might be associated with central nervous disease, but if more often dependent upon disorder of the bloodvessels.

One of the ablest of recent authors on this subject, H. Strauss,<sup>2</sup> writing in 1905, proposes to substitute for the term *Raynaud's disease* the designation *Angiospastic gangrene*. According to this author, the gangrene is rarely symmetrical, and is the result of malnutrition due to ischemia or spastic cyanosis. Raynaud's disease, far from being a trophoneurosis, is, according to Strauss, a pure angioneurosis occurring either as an independent form of disease or in association with some central nervous affection. In this view I heartily concur.

In the interpretation of erythromelalgia there has been a great diversity of opinion. Efforts had been made to attribute it to changes in the posterior gray matter of the spinal cord (Eulenburg,<sup>3</sup> Auerbach,<sup>4</sup> and others), as though the dignity of the disease demanded such an explanation. I do not deny that such may be the case, but a large experience has taught me that the cases associated with spinal symptoms of any sort are few and far between. By degrees, the views advanced chiefly by American writers (Weir Mitchell,<sup>5</sup>

<sup>1</sup> Read in connection with the following paper by Dr. L. Buerger, at the meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1908.

<sup>2</sup> Archiv f. Psychiatr., etc., vol. xxxix, p. 109.

<sup>3</sup> Neurol. Centr., 1893, p. 657; Deutsch. med. Woch., 1893, p. 1325.

<sup>4</sup> Deutsch. Zeit. f. Nerven., 1897, vol. ii, p. 143.

<sup>5</sup> Philadelphia Med. Times, 1872; also Mitchell and Spiller, AMER. JOUR. MED. SCI., January, 1899; also Clinical Lecture on Nervous Diseases, Philadelphia, 1897.

Sachs and Wiener,<sup>6</sup> Hamilton,<sup>7</sup> Barker,<sup>8</sup> and others) have obtained general credence. The spinal origin of erythromelalgia is now defended less warmly, and the question to be decided is whether or not these various forms of vasomotor and trophic disturbances, including the acrocyanosis chronica, with or without gangrene (Barker), are invariably of purely vasomotor origin, and whether, even when associated with symptoms of an undoubted spinal character (tabes, etc.), they are not due to the accompanying peripheral vascular disturbance rather than to spinal disease.

The continued study of this subject has been fairly forced upon me by the unusually large number of cases of this description that I have seen in the surgical and the neurological services of Mount Sinai Hospital, while some of the most interesting forms have been observed in private practice among patients of all creeds and classes. So far as the hospital cases are concerned, it is probable that malnutrition, premature arteriosclerosis, and the peculiar occupations (tailoring, sewing-machine work—all of them involving, as can readily be understood, a retardation of the venous circulation) are responsible for the frequent occurrence of these special disorders. My dermatological friend, Dr. Lustgarten, is firmly convinced that a large majority of these cases are due to syphilitic disease. While it may be true that a very large number of the hospital patients whom we have seen have had constitutional syphilis, I must state emphatically that in such cases as I have observed, and in which I have made a thorough inquiry and examination to prove or disprove the presence of constitutional syphilis, I have in rare instances only been able to satisfy myself on this point. Moreover, yielding to Dr. Lustgarten's opinions, I have given deep sublimate injections, in many of the cases without satisfactory results, although Dr. Lustgarten reports verbally to me that he has seen a number of the cases get well after antisymphilitic treatment. Many of these disorders are subject to spontaneous improvement, and the majority of the incipient cases do fairly well on rest alone. I am under the strong impression that rest in bed, with the foot elevated, and the application of heat, by favoring the return circulation of the blood, do more to improve the clinical conditions than any severe or thorough antisymphilitic treatment could accomplish.

Ample opportunity has been afforded us not only for the clinical study of all these conditions, but for an exhaustive analysis of the underlying morbid states. These studies in pathology have been carried on by Dr. Buerger.<sup>9</sup> He will not need me to stand sponsor for his conclusions, interesting as they will prove to be to those concerned with the clinical aspects of various acroneuroses. The important point is that the studies have revealed in these disorders a

<sup>6</sup> Philadelphia Med. Jour., June 29, 1901; also Mt. Sinai Hosp. Rep. for 1898.

<sup>7</sup> Jour. of Nerv. and Men. Dis., vol. xxxi, No. 4, p. 21.

<sup>8</sup> Ibid., 1907, p. 653.

<sup>9</sup> See the following paper.

striking interference with the peripheral blood-supply, thus fully corroborating and amplifying the findings of Wiener and myself in these diseases, as published seven years ago. So far as we have been able to determine up to the present time, the anatomical changes are very much the same in the various clinical groups. Whether or not special anatomical conditions may at some day be assigned as a basis for special clinical types will have to be left to future consideration. According to Dr. Buerger's studies, the morbid changes are the same whether the cases be designated clinically as erythromelalgia, Raynaud's disease, or acrocyanosis.

If we were to adhere rigidly to the descriptions of the disease as originally presented by Raynaud, or to the description of erythromelalgia as given by Weir Mitchell, we should no doubt be compelled to exclude some of the cases herein referred to. While it is not wise to depart too widely from the type as described by its discoverer, we must make allowance for variations that occur from a type and for the broadening studies of later years. Thus, as Strauss mentions, if we insisted on a symmetrical distribution of gangrene in Raynaud's disease, we should often be compelled to make a different diagnosis in cases in which all other symptoms point to the existence of this affection; and similarly, as I pointed out some years ago, it will not do to eliminate from the category of erythromelalgia all cases in which wet or dry gangrene occurs at some stage of the disease, although Weir Mitchell insisted that this absence of gangrene was one of the points of differential diagnosis between erythromelalgia and Raynaud's disease. I am confident that Dr. Mitchell himself will yield this point, since there are many cases of undoubted erythromelalgia in which gangrene has developed.

The special value of these clinical studies has been not merely in calling attention to the various forms of vasomotor and tropho-neuroses, occurring in the upper and lower extremities, but the study of them has helped to rivet attention upon the disorders resulting from deficient blood supply of the extremities, and, among other things, the examination of the pulsation of the dorsal artery of the foot has become almost as important a part of the general physical examination as is the routine examination of the radial pulse.

In summarizing clinically the experiences of recent years, I wish to emphasize a number of points; in submitting clinical proof, I have, so far as possible, endeavored to utilize some of the histories of patients in whom the amputation of diseased portions of the extremities has given Dr. Buerger the opportunity to make his excellent pathological studies.<sup>10</sup> The points especially to be emphasized are these:

1. Erythromelalgia and Raynaud's disease are often associated with one another; a sharp line of demarcation between the two

<sup>10</sup> I have purposely avoided giving the histories of text-book cases.



cannot always be maintained; and the types blend into one another so readily that the exact labelling of a case is often a matter of great difficulty.

2. The clinical symptoms at one part of the disease correspond closely to the erythromelalgic type, and at a later stage to the Raynaud type.

3. Erythromelalgia is relatively frequently associated with gangrene, generally dry gangrene.

4. There are cases which, in their incipiency, present typical symptoms of Raynaud's disease, and as they progress might very well be designated cases of spontaneous gangrene due to obliterating endarteritis (or angiothrombosis—Buerger). In the following cases these various points are well illustrated:

CASE I.—S. R., a cigarmaker, aged fifty-seven years, was admitted to the hospital, January 28, 1907. Both his parents died of Bright's disease. He had been a very hard worker, but was well enough until three years ago when his foot became very sensitive to cold. About a month prior to his admission the patient felt pain radiating down the back of right thigh and leg. When the feet were dependent they became livid and cold. After a brief stay in the hospital he was much improved and requested his discharge. He was readmitted June 28, 1907. At this time his left leg was more affected than the right. Both feet were tender on slightest pressure. When they hung over the edge of the bed they became erythematous from the soles to the upper level of the malleoli. The veins stood out prominently in contrast with the vivid red of the skin. If the feet remained in the dependent position, they became cyanosed up to the knees, and erythematous spots of irregular outline appeared over both knees. No pulsation could be felt over either dorsal pedal artery. The left fifth toe was in a state of dry gangrene. After much hesitation on the part of the surgeons, amputation above the left knee-joint was performed. The patient developed delirium three days later, which was followed by coma and death. There was no evidence at any time either of diabetes or of central nervous disease. No autopsy was granted; but Dr. Buerger examined the amputated limb, which yielded typical changes in the bloodvessels.

CASE II.—A. P., laborer, aged forty-nine years, was admitted to the hospital April 5, 1907. Eight years ago he had a burning pain in the fourth and fifth fingers of the right hand which extended up to the shoulder. After six months the pains ceased. One year ago he began to notice a burning sensation over the dorsum of both feet in walking; the feet always felt cold. On examination we found slight cedema of both legs; the toes of both feet were blue; on the outer aspect of the left foot were two ulcers. When the feet were in dependent position the toes became violaceous in color and excessively painful. After a few weeks the big toe of the left foot presented a small dark spot, which gradually developed into an increasing area

of gangrene for which amputation was performed by Dr. Lilienthal about a month later. The amputated limb was examined by Dr. Buerger. The patient made a good recovery.

In this case most of the symptoms were those of the Raynaud type; although in general appearance and behavior there was a distinct resemblance to the limbs as seen in some conditions of erythromelalgia. The histological findings were in all respects like those of our first case.

CASE III.—H. R., a travelling salesman, aged thirty-five years, was seen in consultation September 25, 1907. He denied syphilis, but had been a hard worker since the age of thirteen years. Five years ago he felt severe pain in the big toe of the left foot. After two weeks the nail of this toe came off, and a large ulcer developed on the outer surface of the foot. This ulcer healed; at the same site another ulcer had formed; during the last six weeks the ulcer had grown much larger. This patient got relief when the foot hung downward; while he was in bed the foot was numb and painful. During the examination it was noted that the entire left foot was swollen, red, and extremely painful; the patient was comfortable only when his knees were crossed and when he clasped the foot firmly in his hands. There was a large ulcer of the big toe of the left foot with exposure of the bone. All the other toes were intensely livid. The pulse could not be felt over the dorsal, the popliteal, or the iliac arteries. The pulses in the right lower extremity were equally deficient, except that the right iliac pulse could be felt. There was no evidence of nephritis or of diabetes. Amputation was advised. Such a case as this might well be designated as one of spontaneous gangrene, although the resemblance to erythromelalgia was undeniable. The evidences of widespread arterial disease, the greater pain in the recumbent position, and the early ulceration are of especial interest.

CASE IV.—J. L., a clothing presser, aged forty-seven years, was seen by me at the hospital (Dr. Lilienthal's service) in November, 1906. The only facts of importance in his history were that he had worked as a foreman in a Russian forest fourteen hours per day, and that his hands and feet had been frozen frequently. He was a heavy smoker and a moderate drinker; there was no evidence of syphilis. His present illness dates back about eight years, when he began to complain of drawing pains in both calves. This was worse after standing for any length of time, and especially on walking. Later on, pain set in in the soles of both feet ("flat-foot pains"). About five years ago he began to complain of cold feet; said his feet were bluish in color after standing, and that there were drawing pains in toes of left foot. The second toe of left foot was amputated about five years ago on account of progressive sloughing. Three years ago the second toe of the right foot underwent dry gangrene; three months ago the fifth toe of the right foot met a similar fate. Six months ago

he began to complain of drawing pains in both hands, and noticed a bluish discoloration. The tip of the middle finger of the left hand began to turn black two months prior to my examination. At this time the records showed: A peculiar pinkish coloring of all the finger tips; the tip of the middle finger of the left hand is painful; a small portion of the pulp of the right middle finger has sloughed away. The grasp is good, sensation normal in both upper extremities, and both radial pulses are of fair quality. When the hands are held high above the head the finger tips become much paler, and it takes a long time for the pinkish color to return after the hands have been lowered. In the lower extremities the ravages of the disease are particularly noticeable. The second and third phalanges of the second toe of right foot have fallen off; the middle toe has been amputated; the tip of the right little toe is black and gangrenous; other toes are blue. The tip of the last phalanx of the left large toe is missing. The second toe has been amputated. Pain is not increased when feet are in a dependent position, except that there are pains occasionally in the heels. All reflexes and sensation are normal; pulsation cannot be felt either in the dorsal arteries of the feet or in the posterior tibial arteries. In spite of the inroads made by the disease, after a stay of one month in the hospital, under general tonic and stimulating treatment, the patient was discharged "improved." It is worth noticing as etiological factors, in this typical instance of Raynaud's disease, the exposure to cold, the excessive use of tobacco, and the long hours of work. The process was relatively destructive, but remained limited to the finger tips and toes.

5. I wish to call attention to the occasional association of Raynaud's disease with chronic rheumatism, and to its occurrence in cases of cerebral endarteritis. It is almost superfluous to point out the relation in these cases between the defective blood supply of the extremities and the cardiac and vascular disease accompanying these disorders. The following case may be cited to illustrate this point:

CASE V.—Mrs. M. F., aged fifty-seven years, was seen April 23, 1900. She has had chronic articular rheumatism, and has presented all the symptoms of mitral stenosis, with occasional deficient compensation. At the time of my examination the patient was much troubled by attacks of pain in the upper extremities, the finger tips becoming blanched and the nails turning blue, without any acute heart disturbance to account for such changes. Such attacks would last for several hours and would then disappear. On one occasion a note was entered on my records: "Fingers swollen, glossy, livid, and nails very blue." From May 20 on, for a period of about one month, the hands were invariably blue in the dependent position, the fingers glossy and painful. After treatment by the use of hot baths for the hands, massage, and nitroglycerin, the condition was much improved. This same patient had an attack of left hemiplegia five years previously. I have not seen the patient for

several years, but understand that up to the time of her death, a few months ago, the vasomotor disturbances in the upper extremities did not recur.

6. Special attention should be directed to the association of intermittent claudication with symptoms of the Raynaud type, an association which was theoretically conceived a number of years ago both by Erb and myself, but which I have seen demonstrated in only a few instances. Erb proved conclusively that intermittent claudication is due to interference with the peripheral blood supply, and in my first paper on erythromelalgia I stated that from the viewpoint of pathology, "intermittent claudication may be contrasted with erythromelalgia (motor paralytic symptoms with sensory and vasomotor disturbances, both due to peripheral nerve disease following upon obliterating endarteritis)." If Dr. Buerger's views are correct, we shall have to substitute "thrombo-angiitis" for "obliterating endarteritis."

CASE VI.—Mr. E. R., aged fifty-five years, was seen by me in consultation with Dr. Joerg, of Brooklyn. Patient has the appearance of a man in good health. He states distinctly that until seven years ago he was able to climb high mountains, but found in the last four years that his right calf was painful after walking, and has had calf-spasms for many years. About a year ago he noticed the same pain in the left leg. The pain begins in the dorsum of the foot and travels up the leg as far as the knee. After lying in bed for one hour the pain disappears. During the past few months he feels completely exhausted after walking for about fifteen minutes. After the lapse of this period the legs give way, and he has a feeling of being almost completely paralyzed. After a few hours' rest he feels that he would be able to walk miles, but whenever he has walked ten or fifteen minutes the power of the legs seems to give out. On examination it was found that both feet were blue, particularly the left; toe nails blue; his hands were also livid. He has periods in which the fingers are absolutely white and numb, and he has to rub them very vigorously. Of late he has noticed the same in the toes. He has considerable pain during these periods, both in the fingers and toes. The left knee-jerk is slightly livelier than the right, but there is no ankle clonus on either side, a very slight Babinski occasionally on the left. No dorsal pulse can be felt, and no popliteal. He has a general arteriosclerosis.

There can be no doubt that in this case there is a distinct intermittent claudication, though not as advanced or as complete as in some other cases, and with this is joined distinct evidence of disturbances in peripheral circulation, both in the hands and the feet, resembling in every way the symptoms of Raynaud's disease. The association of these two groups of symptoms points indubitably to the fact that the changes in the bloodvessels of the upper and lower extremities are responsible for both groups of symptoms.

# **THROMBO-ANGIITIS OBLITERANS; A STUDY OF THE VASCULAR LESIONS LEADING TO PRESENILE SPONTANEOUS GANGRENE.<sup>1</sup>**

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THERE is an interesting group of cases characterized by typical symptoms which the Germans have described under the name "Spontan-gangrän." In 1879 von Winiwarter published the results of the pathological findings in one case, and reported an obliteration of practically all of the arteries of the leg by reason of a chronic proliferative process, due, in his opinion, to a new growth of tissue from the intima. He, therefore, proposed a new name for this condition, namely, "endarteritis obliterans." Patients afflicted with this so-called endarteritis obliterans present symptoms which are so characteristic that the diagnosis is not difficult. I have had occasion to observe some thirty cases of this disease, and have made pathological studies on the vessels obtained from eleven amputated limbs.

The disease occurs frequently, although not exclusively, among the Polish and Russian Jews, and it is in the dispensaries and hospitals of New York City that we find a good opportunity for studying it in its two phases, namely, in the period which precedes and in that which follows the onset of the gangrene. We usually find it occurring in young adults between the ages of twenty and thirty-five or forty years, and it is because the gangrenous process may begin at an early age that the names presenile and juvenile gangrene have been employed. In one class of cases there are rather characteristic attacks of ischemia. The patients complain of indefinite pains in the foot, in the calf of the leg, or in the toes, and particularly of a sense of numbness or coldness whenever the weather is unfavorable. Upon examination we see that one or both feet are markedly blanched, almost cadaveric in appearance, cold to the touch, and that neither the dorsalis pedis nor the posterior tibial artery pulsates. When the foot becomes warm some color gradually returns. Some patients complain of rheumatic pains in the leg, others are able to walk but a short distance before the advent of paroxysmal shooting, cramp-like pains in the calf of the leg makes it imperative for them to stop short in their walk. Some of these cases give the typical symptoms of intermittent claudication. After months—or, in some cases—even years have elapsed trophic disturbances make their appearance. It is at this stage that another rather unique symptom makes its appearance: one which gives the foot the appearance

<sup>1</sup> Read at a meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1908.

typical of erythromelalgia. In the pendent position a bright red blush of the toes in the anterior part of the foot comes on rather rapidly, extending in some cases to the ankle or slightly above. Soon a blister, hemorrhagic bleb, or ulcer develops near the tip of one of the toes, usually on the big toe, frequently under the nail, and when this condition ensues the local pain becomes intense. Such trophic disturbances may at times make little progress and last for months; sometimes, however, the skin in the neighborhood shows cyanotic discoloration, and dry gangrene of the whole toe is an early issue. Even before the gangrene, at the ulcerative stage, amputation may become imperative because of the intensity of the pain. The left leg is usually the first to become affected, although both limbs may show vascular disturbances almost simultaneously, and, when such is the case, the trophic changes, the ischemia or the reddening may give rise to a symptom-complex, often diagnosed as Raynaud's disease. In short, after longer or shorter periods, characterized by pain, coldness of the feet, ischemia, intermittent claudication, and erythromelalgic symptoms, evidences of trophic disturbances appear which finally pass over into a condition of dry gangrene.

**HISTORICAL.** Although the literature bearing upon the pathology of the disease just described is large, I wish to call attention only to some of the more important contributions. Von Winiwarter and Friedländer ascribed the closure of the vessels to a proliferation of the cellular and fibrous elements in the intima, and therefore proposed to call the lesion by the name "endarteritis obliterans." This theory has been accepted by most authors, and even to-day, it is to be found in all the text books. Somewhat later, Wilonski pronounced the opinion that the essential change in the vessel walls was due to a multiplication of the elastic fibers, and proposed the name "arteritis elastica" for the condition. Perhaps the most important contributions are those of Weiss and Zoege von Manteuffel, because these authors placed an entirely new interpretation upon the pathological findings. Basing his paper upon the studies of his assistant Weiss, von Manteuffel suggests that the extensive occlusion of the vessels in this disease is dependent upon a primary arteriosclerosis; that the obliterative process commences in the popliteal artery, where it owes its inception to the formation of a parietal white thrombus; and that by virtue of a gradual extension of the parietal thrombus downward, followed by organization, a picture resembling an obliterative endarteritis is produced. In his cases the veins did not seem to be involved in the process. Von Manteuffel comes to the conclusion that the thrombosis is due to desquamation of endothelial cells, and that this occurs where the intima shows most advanced lesions of arteriosclerosis, namely, somewhere in the popliteal artery. In spite of the views expressed by these latter authors, Sternberg, from the study of eight cases, is in accord with the old conception first suggested by von Winiwarter. Bunge, on the other hand, agrees with

von Manteuffel, but his three cases appear to be instances of advanced arteriosclerotic change in elderly people rather than examples of the disease grouped under the name "endarteritis obliterans."

Two schools, then, have arisen among those who have made careful anatomical investigations: first, those who agree with von Winiwarter and who attribute the closure of the vessels to proliferation of the intima; and second, those who consider the process to be a peculiar type of arteriosclerosis in which desquamation of endothelium in the popliteal artery leads to the formation of parietal white thrombi and to occlusion of the arteries by direct peripheral extension from the primary focus.

During the last year and a half, through the kindness of Drs. Lilienthal, Gerster, and Sachs, of the Mt. Sinai Hospital, I have been able to make careful anatomical studies on eleven amputated lower extremities.<sup>2</sup> Although the results of the macroscopic and microscopic examination of the vessels agreed in part with the findings of other authors, a large number of additional facts were obtained which throw new light upon the pathology of the process. I may anticipate now by saying that from my own findings I can not agree with the views of von Winiwarter or von Manteuffel, but have come to the conclusion that we are dealing here with a thrombotic process in the arteries and veins followed by organization and canalization, and not with an obliterating endarteritis.

**GROSS PATHOLOGY.** If we dissect out the vessels in these cases, we are struck by the fact that there is an extensive obliteration of the larger arteries and veins. Besides this, we find two other lesions which vary greatly in their intensity, namely, the periarteritis and the arteriosclerosis.

Upon making a large number of sections through such obliterated arteries and veins at different levels, we find certain characteristic appearances, which, in a general way, depend upon the age of the occluding process. Usually the vessel is seen to be filled with a grayish or yellowish mass that can be distinctly differentiated from the annular wall of the vessel, and that appears to be pierced at one point (more rarely at a number of points) by an extremely fine opening through which a minute drop of blood can be squeezed. Such obturating tissue is firm in consistency, and does not at all resemble the crescentic or semilunar occluding masses typical of arteriosclerosis. The vessel itself is usually contracted, so that its wall appears somewhat thickened. This picture is characteristic of arteries or veins which are the seat of a very old obliterative process, and is to be found most frequently in the peripheral portions of the vessels, although at times this type of lesion may extend throughout the whole length of the vessel, from the dorsalis hallucis almost into the popliteal.

<sup>2</sup> Since reading this paper eight additional cases have been studied.

As we trace certain of the obliterated arteries or veins upward, we are apt to meet with a change in the character of the obturating tissue. Frequently it becomes softer, more brownish in color, and terminates abruptly in the lumen of an apparently normal vessel; at other times the brownish tissue gives way to soft reddish masses which are evidently the results of recent thrombosis. In some cases this thrombotic process occupies large portions of the vessel's course; in others, it is of short extent and terminates in a long cone of recent thrombus.

It is interesting to note that the veins share equally with the arteries in the lesion of occlusion. In some cases the veins are more extensively involved than the arteries, and this is particularly true of the collaterals of the posterior tibial, which are often closed when the anterior tibial veins are open. As for the arteries, we usually find an obliteration of a part or the whole of the anterior tibial, of the dorsalis pedis, and dorsalis hallucis, an occlusion of the posterior tibial and plantar vessels, with or without involvement of the peroneal. Sometimes the anterior tibial is practically normal in its upper half or upper two-thirds. More rarely a large portion of the dorsalis pedis is open, with the beginning of the occlusion in the upper part of this vessel or in the lower part of the anterior tibial. It is to be regretted that the termination of the process in the posterior vessels of the leg could not be determined in every instance because of the fact that amputation was done at a point where the posterior tibial was closed. In two cases, however, the popliteal and part of the posterior tibial vessels were found free; in others the popliteal could be felt to pulsate before the operation, and we can therefore conclude that in a number of cases at least the obturation does not attain the level of the popliteal artery.

Without giving a detailed description of the extent of the occlusion in all the cases, I may summarize by saying that we usually meet with obliteration of large territories with closure of the distal parts of the vessels, rather than the proximal; that there is often an involvement of some of the smaller branches, such as metatarsal and tarsal, but that the smallest arteries are free. The beginnings of the obliteration are not to be sought in the capillaries nor in the finest branches. If we follow the vessels upward, we frequently see a sudden cessation of the process, and in a number of instances we find that some 5 or 10 cm. of a vessel's length is closed and that the portions above and below are apparently normal.

It is from a study of the terminations of the obliterating masses of tissue, together with a study of those parts of the vessels which are apparently unaffected by the process, that most valuable information in regard to the pathology of the disease can be gained. As already indicated, there may be a sudden and abrupt change from occluded vessel to normal vessel; that is to say, the yellowish-brown tissue terminates in a rounded dome-like process which projects into



an apparently normal lumen, or there may be a transition into red thrombotic masses or a conversion of the denser occluding tissue into tissue not unlike granulations. Such terminations occur at various points in the course of the arteries and veins. In one case the obliteration of the anterior tibial extended to about the middle of its course, and above this point its walls were almost normal save for some thickening of the intima. In another case the upper and lower terminations of the occluding tissue were found in the posterior tibial and in the peroneal arteries.

The peculiar appearances presented by these terminations, the apparently normal condition of the vessel above and below the occluding masses, and the transition into thrombosed areas, all speak in favor of the view that we are dealing with a thrombo-arteritis or thrombophlebitis, rather than with a proliferative or obliterating process derived from the intima of the arteries and veins. The microscopic studies gave sufficient evidence of the correctness of this conception.

Besides the lesion of occlusion there are two other striking changes, namely a certain amount of arteriosclerotic thickening and peri-arteritis. The arteriosclerosis is never pronounced except in those rare instances in which the patient has suffered from the disease for many years and has reached the latter part of the fourth decade. As a rule, we note but a very slight degree of whitening or thickening of the intima here and there in the patent portions of the vessels. In a very few cases small atheromatous patches are present. There were deposits of lime in but one case, and these were of small extent.

A much more interesting and more important change is the fibrotic thickening of tissues immediately about the vessels, which I wish to discuss under the term "peri-arteritis." Wherever the vessels are occluded there is apt to be an agglutinative process which binds together the artery and its collateral veins, and sometimes also the accompanying nerve, so that liberation of the individual vessels by dissection is difficult. This adhesive condition is due to fibrous tissue growth, and varies considerably in its amount. At times we find little or no change about the occluded artery, at times fairly firm agglutination of the vessels in the sheath without much fibrosis, and at other times, so large an amount of connective tissue growth that isolation of the vessels or nerves becomes impossible, and the vascular structures make up one dense rigid cord. In a general way we may say that whenever both the collateral veins and the artery are occluded, we expect a fair amount of peri-arteritis, and that when but one vessel is affected, the perivascular change may be insignificant; and finally that the amount of peri-arteritis varies in the different cases as well as in the different territories affected by the disease.

**HISTOLOGY.** The pictures presented by the vessels that are involved in this process are so varied, that I must confine myself to the description of those rather typical changes that have

suggested the true nature of the process to me, and from a study of which we can see the development of the lesion from its incipency to its final maturation. I wish to point out: (1) The lesions of arteriosclerosis; (2) those that belong to the peri-arteritis; (3) the typical pictures found in the old obliterative process; (4) the differentiation of this lesion from the occlusive changes of arteriosclerosis; and (5) the various stages in the development of the occluding process from the beginning of the thrombosis to the final filling up of the vessel with dense fibrotic masses.

Both the arteries and the veins show varying degrees of thickening of the intima, the usual subendothelial changes with a fairly well marked hypertrophy of the internal elastic lamina without much proliferation of new elastic tissue in the thickenings of the intima. Of the two types of elastic tissue production pointed out by Jores, that which is dependent upon reduplication or hypertrophy of the internal elastic lamina is the more pronounced. Now and then in the older patients there are small plaques. Although the very small arteries may also be the site of thickening of the intima, this change is never sufficiently great to lead to complete or even marked obliteration of the lumen of the vessel. In the popliteal artery the formation of nodular thickenings is most extensive, but even here these are of moderate size.

The perivascular changes manifest themselves in a proliferation of connective tissue, in and around the adventitia, and are of two types, recent and old. Where the perivascular proliferation is active, the fixed connective tissue cells multiply and fibrous intercellular substance is deposited. Here and there small perivascular foci of lymphoid cells are found, but these do not seem to take an important part in the formation of connective tissue. In the old variety the fibrotic process appears to have come to a standstill, and the vessels and nerves are encased by dense bands of fibrous tissue, sometimes of a hyaline nature.

If we examine a cross-section of an artery or vein which is the seat of an old obliterative process, we often find an irregular, centrally placed lumen, a large amount of new-formed tissue occluding the original lumen, and certain changes in the media, the whole picture giving the impression that there is an extensive proliferation of the intima, namely an endarteritis obliterans (Fig. 1). From a consideration of the descriptions which are to follow, we will understand, however, that the new masses in the lumen are not derivatives of the intima, but owe their origin to organization of obliterating red thrombi. In the occluding tissue we find a fairly large number of capillaries, some blood pigment, and fibrous tissue which is either rich in cells (Fig. 2) or has already become sclerotic in nature. Where the process is oldest, there the capillaries are few, the connective tissue has become dense, the pigment has disappeared, and either in the middle or near the periphery of the obturating mass

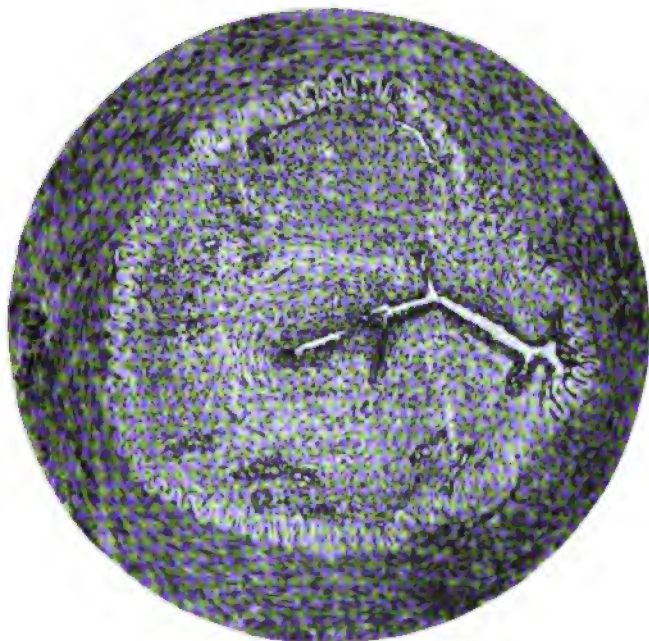


FIG. 1.—Obliterating tissue; old variety in dorsalis pedis; can be mistaken for "endarteritis obliterans;" old connective tissue; canalization; only slight vascularization of media.  $\times 60$ .



FIG. 2.—Obliterating tissue; young variety, in the posterior tibial artery; on the right the vascular young connective tissue with numerous cells and blood pigment; on the left the thickened intima and part of the media.  $\times 250$ .

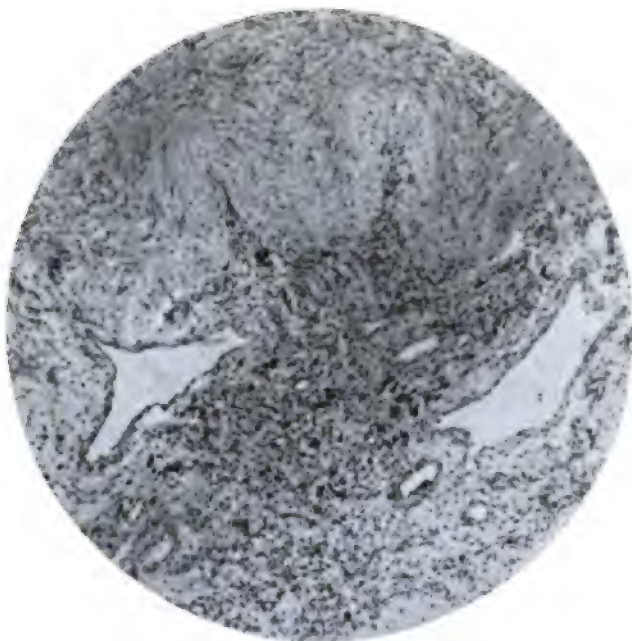


FIG. 3.—Old fenestrated obliterating tissue in the anterior tibial artery; above, the media and intima; below, blood spaces, dense connective tissue, and pigment.  $\times 80$ .

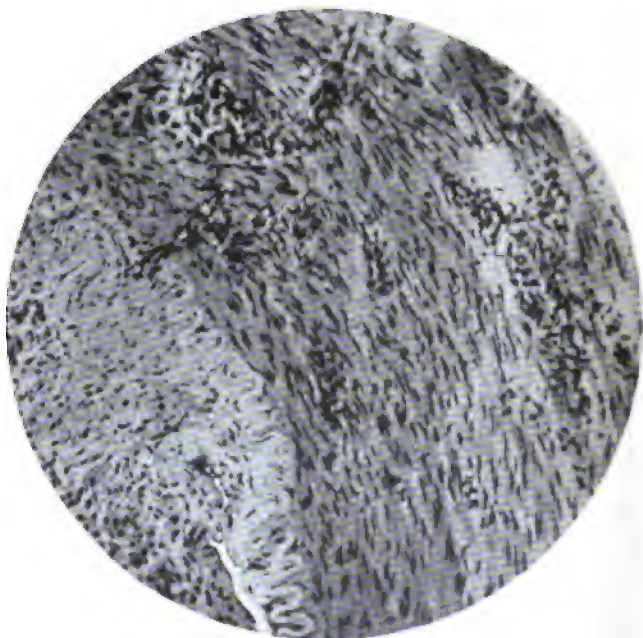


FIG. 4.—Lesions of the media in medium-sized arteries; many capillaries with or without slight perivascular lymphoid infiltration in the media; penetration of the internal elastic lamina by vessels which enter rather old typical occluding tissue.  $\times 125$ .



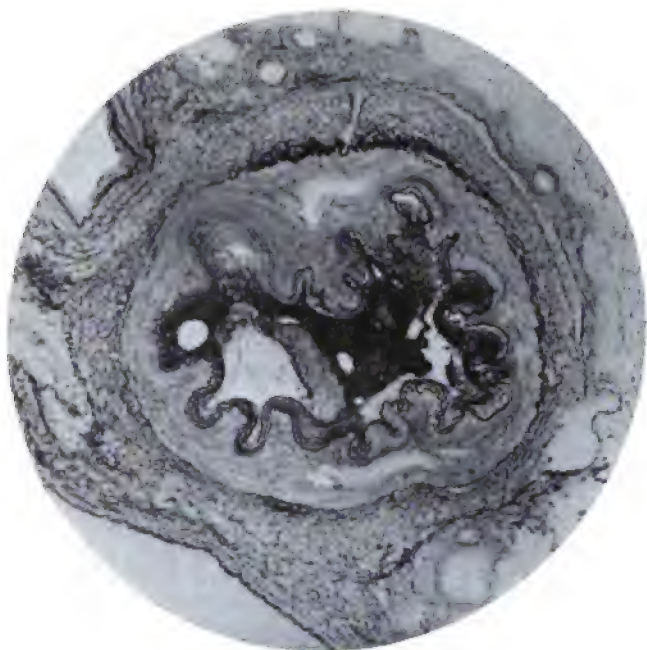


FIG. 5.—Obliterating arteriosclerotic process (orcein). The greater part of the lumen is occluded by tissue arising from the intima, and containing the typical elastic tissue found in arteriosclerosis; the small triangular clear area in the left part of the lumen contains a recent thrombus.  $\times 40$ .

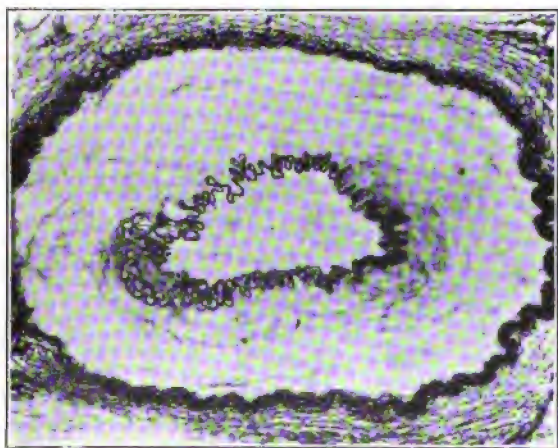


FIG. 6.—Absence of elastic tissue in thrombo-angiitis obliterans (orcein). The lumen is filled by old organized clot; no elastic-tissue production; below, elastic tissue in an arteriosclerotic plaque.  $\times 40$ .

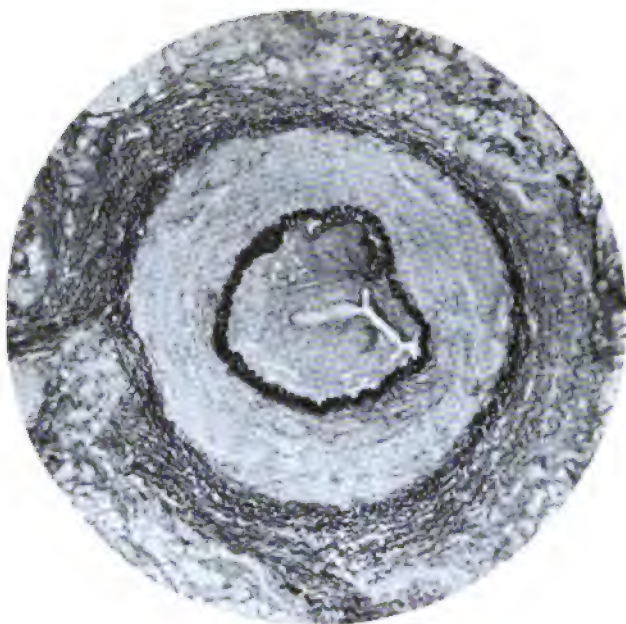


FIG. 7.—Elastic tissue in thrombo-angiitis obliterans. Perivascular disposition.  $\times 40$ .

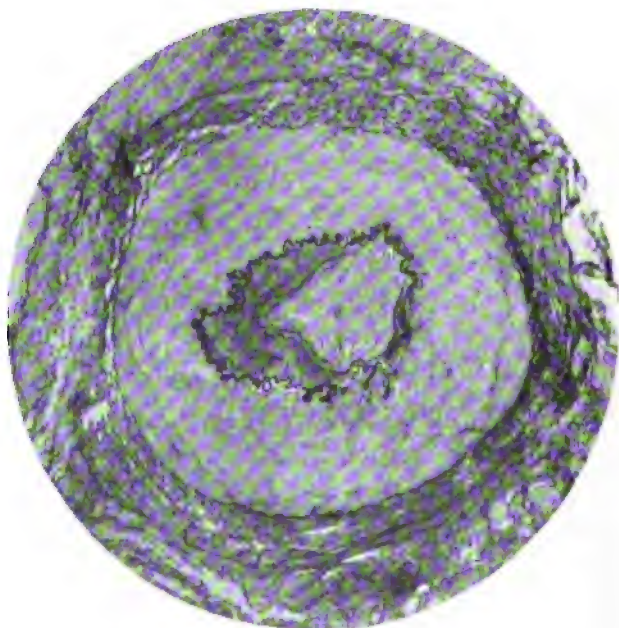
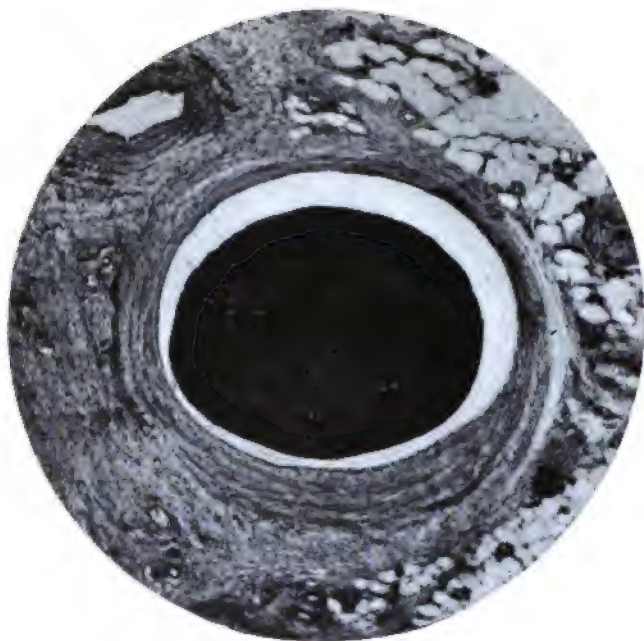


FIG. 8.—Thrombotic process at the site of an arteriosclerotic plaque in the posterior tibia artery; typical elastic tissue in plaque; absence of elastic fibers in the obliterating mass except around certain vessels.  $\times 40$ .



FIGS. 9 and 10.—Red thrombus in anterior tibial vein. In Fig. 9 the termination of the clot (shrunk) lies in a portion of the vessel whose media is normal. In Fig. 10 the organizing process has commenced: the clot is adherent; with it there is the usual vascularization and slight cellular infiltration of the media.  $\times 40$ .



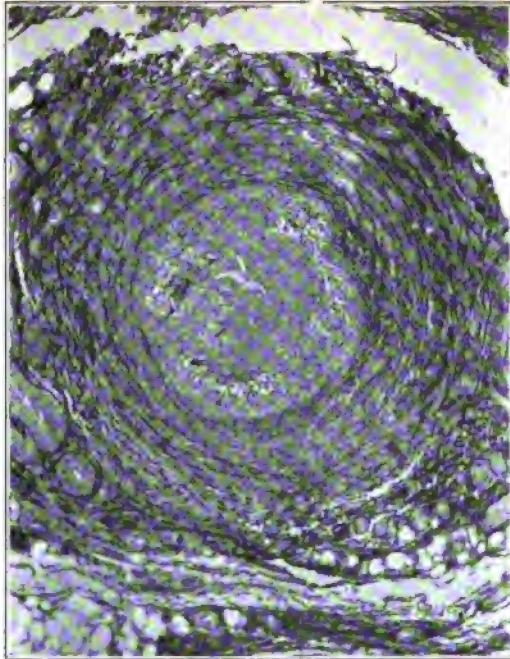
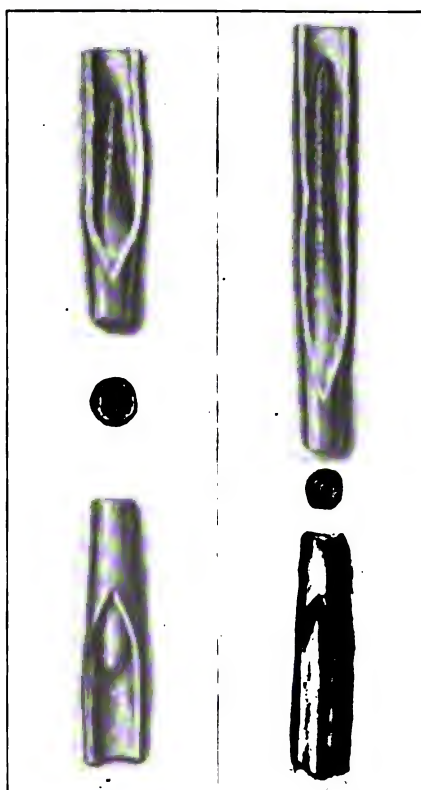


FIG. 11.—Early thrombosis with very slight changes in the media and intima; note the peripherally situated giant-cell foci.  $\times 60$ .





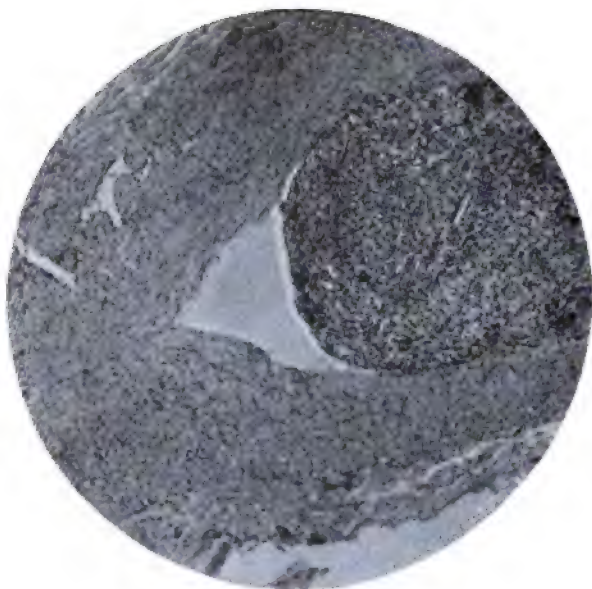


FIG. 13.—Central termination of an occluding mass in the peroneal artery, longitudinal section; vessel collapsed on the left, with the opposed intima layers in contact; the rounded extremity of an organized thrombus fills the distal half of the artery; slight thickening of the intima independent of the obliterating tissue.  $\times 50$ .

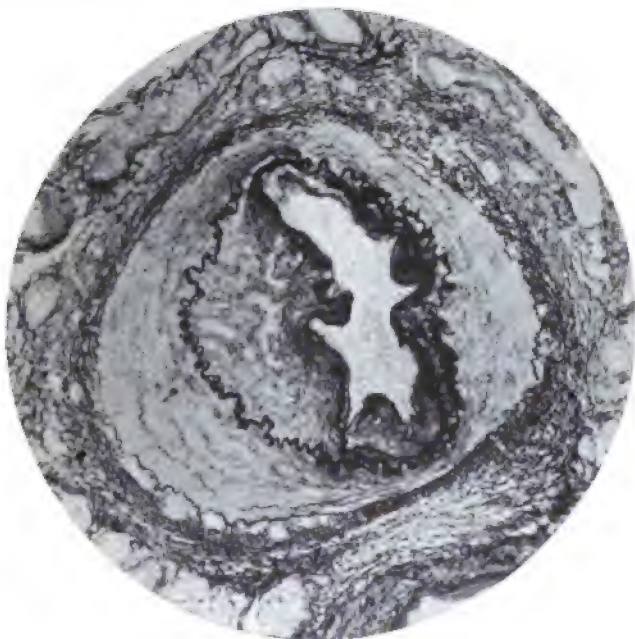


FIG. 14.—Old canalized thrombus giving an appearance similar to that found in obliterating arteriosclerosis; elastic-tissue formation around newly formed vascular channels. Obliterating tissue, which is very old and dense, would show a great many elastic fibers arranged parallel to the internal elastic lamina if the process were arteriosclerotic. The large channels are found to divide into smaller ones at other levels.  $\times 40$ .

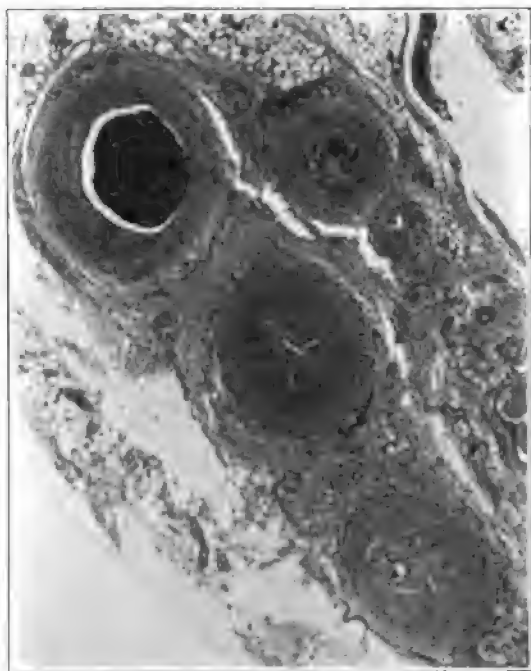


FIG. 15.—Artery and veins showing different stages of the obliterative thrombotic process; above there are two recently thrombosed veins; in the centre and below, an artery and vein are filled with sclerotic canalized tissue.  $\times 18$ .

there is a large dilated vessel which is surrounded by connective tissue and which simulates the remnant of the original lumen. In other vessels there are large sinuses in the occluding mass (Fig. 3), or dilated vessels separated by dense connective tissue; or, there are atypical conformations in which two large blood spaces are separated by a septum that appears to spring from the intima of the vessel. The internal elastic lamina is thrown into marked folds, and between it and the connective tissue described, there may be a slight or moderate amount of fibrotic change in the intermediate layer of Eberth. The striking lesion of the media is the presence of capillaries with or without a small amount of lymphoid infiltration in their immediate vicinity (Fig. 4). Such capillaries may be present in small or in large numbers, depending upon the age of the process; where the occlusion is recent, the signs of activity in the media are striking, the capillaries plentiful, the cellular infiltration marked. The fine vessels come in from the adventitia, pass through the media, and penetrate the internal elastic lamina in order to vascularize the obturating mass.

What are the distinguishing features which enable us to differentiate an arteriosclerotic process from the lesions just described, and how can we establish the independence of the obturating masses from the intima from which most authors would have them arise? By the employment of the elastic tissue stains certain characteristics are brought to light which make it possible for us to say whether we are dealing with a thickening of the intima or with a new tissue lying in the lumen of the vessel. In arteriosclerosis we often find large obturating plaques which almost completely fill the vessel, the small space that is left being finally closed by a thrombus which becomes organized. It is not difficult to recognize such lesions as being arteriosclerotic when we note the large amount of elastic fibers in the plaque and note that these fibers are disposed for the most part parallel with the internal elastic lamina (Fig. 5). In the occluding masses of so-called endarteritis obliterans, we find either a total absence of elastic fibers, or, when such are present, a growth of fibers around the larger canalizing vessels, particularly about those which are thick-walled and old (Figs. 6 and 7).

The differences in the two lesions are well elucidated by the pictures which we obtain when we examine vessels that show a combination of marked arteriosclerosis and so-called endarteritis obliterans. At times we find occlusion of a vessel by obturating masses at the site of an arteriosclerotic plaque, and then the distinctions which I have pointed out become very apparent (Fig. 8). In such places the elastic fibers that belong to the thickened intima do not pass over into the occluding tissue except in those rare instances in which the penetrating vessel has ruptured such elastic fibers and has carried them for a short distance inward.

The most instructive histological pictures are those that are

obtained in an examination of the vessels that are closed by transitional occluding tissue, and by this I mean obturation due to red thrombotic masses which can be traced into the softer brownish tissue and which finally may terminate in the dense old masses, the histology of which has already been discussed. In a number of cases and especially well marked in the vessels in an extremity which was amputated because of pain without gangrene, such transitions from areas of red thrombosis into the older stages were found. If we examine a vein or artery at or near the termination of the red thrombus, we find a fairly recent clot filling the lumen of the vessel without change in the vessel wall (Fig. 9). A short distance farther the clot becomes adherent in places and the corresponding portions of the media show beginning lymphoid infiltration and the earliest signs of vascularization (Fig. 10). At a point still farther removed, the aspect of the thrombosis has considerably changed. A number of miliary foci, not unlike miliary tubercles, make their appearance near the periphery, and there are evidences of organization such as the formation of capillary sprouts, fine capillaries, and fibroblasts (Fig. 11). The miliary foci present a central area of fibrin, and one or more giant cells (probably phagocytic in nature) with cells not unlike endothelial cells in a peripheral zone. Such giant-cell foci are but early stages in the process of organization. At another level the picture changes. The miliary foci gradually become lost, the vascularization of the clot becomes marked, the fibrin is almost absent, and numerous small round cells are scattered throughout. Here the media also shows quite a number of small capillaries with or without perivascular lymphoid infiltration. Whilst the fine vessels in the thrombus at this level are thin-walled, we soon note a change in their character. They become longitudinally disposed, here and there they connect with the media, they are surrounded by numerous round cells and fibroblasts and some blood pigment. These latter pictures correspond to the tissue which appears brownish and is not very firm. From this point on the transition into the old type is fairly rapid. The cells in the obturating mass disappear and the fibrous intercellular substance becomes abundant, some of the capillaries atrophy, others become dilated, forming large spaces with well defined walls; at times there are numerous sinuses giving a fenestrated appearance; at times there is a centrally placed vessel resembling a much diminished lumen of the original vessel, and sometimes such canalizing vessels are centrally placed. With this final maturation of the organizing process there are certain concomitant regressive changes in the media, namely, a diminution in the number of capillaries and the disappearance of alien cellular elements.

A detailed discussion of all the bizarre appearances that were found would take me too far, and I have therefore described only those changes which seem to me to be valuable in elucidating the nature of the occlusion, and which show that this is to be sought

not in an endarteritis, but in the organization of obliterating thrombi. I have given in brief the stages in the development of the process, and have shown how the old typical pictures can be directly traced into the areas of old and recent thrombosis; further how the changes in the media are dependent upon vascularization of the clot and are not primary. What other evidences have we that establish the correctness of our view of the process? A histological study of some of the terminations of the obturating tissue, particularly of the abrupt variety, gives valuable information on this point. Thus if we make longitudinal sections through those rounded ends of occluding tissues which mark the cessation of the process in some of the vessels, we see how the closed portion of the vessel surrounds a vascular mass of young connective tissue and pigment; we note how the end of this mass rounds off, that it seems to be wholly independent of the intima except for points of junction by means of penetrating capillaries, and we are struck by the absence of pathological lesions just beyond the point of closure (Figs. 12 and 13).

We must not fail to interpret the nature of those pictures which would at first sight be mistaken for obliteration due to proliferation of the intima; namely, those in which there is a large canalizing vessel more or less centrally placed, surrounded by a fair amount of elastic fibers (Fig. 14). The paucity of elastic fibers in what would appear to be thickened intima, and the fact that the apparent remnant of the original lumen of the vessel usually divides at other levels into a number of smaller blood spaces, many of which finally communicate with the media, make it evident that we have here simply another product of the organizing thrombotic process.

Before closing the description of the vascular lesions it may be well to allude to some of the very interesting observations that were made in cases in which the thrombotic process was evidently of long duration. Here we frequently find that various stages in the organizing and thrombotic process may be represented not only in different vessels of the limb, but also in the separate members of a vascular sheath. Thus, the posterior tibial artery may be occluded by dense fibrotic canalized tissue through the greater part of its course, one of its accompanying veins showing an intermediate stage, another a very early process (Fig. 15). Still more striking are the appearances that were seen in the posterior tibial vessels of one case. Here the canalizing vessels had become very large and thick walled, and had become affected by the same thrombotic changes that had previously occurred in the parent vessel.

Pictures such as these just depicted not only point out the true nature of the process but are also suggestive of the historical development of the lesion. They tend to show that there are frequent relapses or recurrences of the thrombosis, now in this, now in that vessel, at one time extending upward in a vessel already diseased, at another time affecting even the canalizing vessels themselves.

*The Nerve Lesions.* The study of the nerves in these cases is of considerable importance, both because the symptom of pain is such a constant and distressing one, and because some of the clinical features, such as the red blush of the foot in the pendent position, the transitory ischemia, and the cramp-like sensations in the calf, have all been in turn referred to some spinal or peripheral nerve disturbance.

In general we may say that the nerve lesions are secondary, apparently dependent upon the fibrotic perivascular changes. Thus we find considerable connective tissue proliferation around the nerve bundles, thickening of the perineurium, and even atrophy of nerve fibers wherever the peri-arteritis is marked and where the nerves are intimately connected with the vessels. In such places degeneration of many nerve fibers can be demonstrated by the Marchi method. The oldest perivascular connective tissue proliferation is then usually accompanied by the most intense fibrosis of the nerve sheaths. The popliteal nerve is usually free, as also the internal popliteal; whereas the anterior tibial and posterior tibial are more frequently affected. The cases vary considerably in regard to the amount of nerve lesions. In some, in which the periarteritis is minimal, no change in the nerves could be demonstrated; in others some of the nerves were found embedded in a dense mass of connective tissue. As regards the extent of the process, this corresponds fairly well with the vascular territory which is involved.

**GENERAL CONSIDERATIONS.** Before entering upon a discussion of the genesis of the process, and before giving our views as to the possible etiology, it may be well to recall some of the more important facts that have been developed by the study of the pathological lesions. These may be summarized as follows: Most of the larger arteries and veins of the amputated limbs were found obliterated over a large extent of their course. The obliterative process can be studied at any stage in its development if enough vessels are examined. All stages in the occlusive change may occur in the various vessels of an extremity or at times in the same vessel in different parts of its course. The occlusion of the vessels is effected by red obturating thrombi; these become organized, vascularized, and canalized. The recent red thrombosis may involve large portions of arteries or veins and is not secondary to the gangrenous process. It occurs even when no gangrene is present.

Certain changes in the perivascular tissues, in the adventitia, media, and intima, regularly accompany the occluding process.

There is moderate thickening of the intima; this is never sufficient to cause marked narrowing of the lumina of the vessels, and does not seem to play any considerable role in the genesis of thrombotic process.

The media and adventitia show cellular infiltration and vascularization wherever thrombosis has occurred. The intensity of

the cellular and vascular change seems in general to depend upon the activity of the organization of the clot; however, in some cases it seems to be sufficiently marked to make it appear that the same agent which calls forth the coagulation of the blood is also effective in producing the mesarterial lesion. The occluding masses frequently terminate abruptly in apparently normal vessels. The changes in the media never extend into the walls of the patent portions of the vessels; usually they terminate before the end of the obturating tissue or thrombus is reached; indeed, the dependence of the medial changes upon the organization of the thrombi can be demonstrated in many places.

As a result of the dilatation of a central canalizing vessel, and the fibrous change in the occluding tissue, a picture resembling that due to intense proliferation of the intima may be produced. By means of elastic tissue stains and a thorough study of the vessels at many levels it is comparatively easy to show that the obliterative process has its origin in a thrombus and differs in a number of essentials from the occlusive change due to arteriosclerosis.

From what has been said, we must needs regard the views of von Winiwarter and those who have agreed with him as fallacious, and have but to deal with the theory propounded by von Manteuffel. We would at first hand be led to the belief that the changes in the intima are in great part responsible for the thrombosis; for this is doubtless the case in the secondary closure by clot in cases of senile and diabetic gangrene. Zoege von Manteuffel takes the view that parietal white thrombi first lodge in the popliteal and gradually extend downward; that they remain mural in nature, are of the white variety, and are but rarely mixed with small red clots of recent origin. Practically every one of my cases furnished me with many evidences of the incorrectness of this conception. Thus, the large territories filled with red thrombi with their transitions into the old occluding masses, the frequent absence of any change in the upper parts of the anterior and posterior tibial arteries when very distal parts were occluded, and further, the presence of pulsation in the popliteal artery in some of the cases in which that vessel could not be examined, all speak against his assumption. We gain the impression that the obturation ascends rather than descends; for the firmest and oldest tissue is most frequently found in the distal parts and not infrequently terminates in young thrombi or soft rounded abrupt terminations in the middle or lower part of the leg. Finally, the presence of the same lesion in the veins, which Zoege von Manteuffel had evidently not encountered, could certainly not be explained in the light of his theory.

What then causes the extensive thrombosis of the veins and arteries? We are not able at this juncture to give a decisive answer on this perplexing point. Even to this day the determining causes of thrombosis are not completely understood, and it is therefore not

surprising that here also we meet with difficulty. A number of factors must be taken into account, the arteriosclerotic change, the lesions of the media, the periarteritis, as pathological changes conducive to thrombosis; the external influences, as well as possible toxic conditions of the blood. We have already alluded to the fact that the changes in the intima do not appear to be responsible for the thrombosis. According to Lubarsch in his very recent summary of the literature on thrombosis, we must regard the changes in the intima as playing but a subsidiary role in this process; for, up to the present time it has not been clearly demonstrated that the endothelium contains any substance that can inhibit coagulation, nor has it been proved conclusively by animal experimentation that lesion of the intima alone suffices for the production of clot. Then again it is common occurrence to find extensive ulcerations and even calcareous plaques without the formation of thrombi. Even more significant is the fact that in arteriosclerosis the most extensive changes in the walls do not correspond to the site of thrombus formation.

In the vessels under consideration this independence of arteriosclerotic thickening and obliterating thrombosis is well illustrated, for in no place were we able to refer the origin of a clot to the presence of a thickened or diseased intima. Indeed, the popliteal artery which is apt to show the most marked arteriosclerotic change, is frequently free and patent. It becomes occluded only when the process has extended upward from its branches. Further, we frequently find complete occlusion of the vessels whose walls are practically normal; and above and below such points the intima of the patent vessel may show a fair amount of arteriosclerosis. The white parietal thrombi which von Manteuffel claims to have seen adherent to arteriosclerotic patches, were never met with in the very great number of sections which we studied. On the other hand, it would appear that some of the thickening of the intima could be attributed to the process of organization of the thrombi, and we believe it to be, in a measure, secondary to that process.

It is not my purpose to enter deeply into a discussion of all the factors that may be responsible for the thrombosis, for my studies on this particular phase of the subject are still incomplete. It is of considerable importance to determine what role syphilis may play in the production of the lesions. A history of this disease was not obtainable in a single case, and thus far I have been unable to demonstrate *Spirocheta pallida* in any of the sections.<sup>3</sup> However the periarteritis is rather suggestive, and requires further investigation. In a number of the cases cultures were made particularly from those portions of the vessels which showed the most active changes, and also from the hard sclerotic occluded portions, with

<sup>3</sup> The final results of this investigation will be reported at a later date.



negative results in every instance. It would seem therefore that at least the pathogenic bacteria are not present.

If we take a broad view of the pathological lesions, we see that we are dealing in main with the results of a healed process, namely, with vessels obliterated by dense connective tissue which has become canalized. In such vessels the thrombotic changes have disappeared, the cellular infiltration and vascularization of the media have diminished in intensity, leaving but a few capillaries behind; and the adventitia and peri-arterial tissues are either slightly thickened or converted into dense connective tissue. Besides this, however, there is the active process, that in which the thrombosis is recent. This is apparently of two varieties. In one of these the vessels are filled with blood clot over a large portion of their extent and there is active organization accompanied by that very slight cellular infiltration and capillary invasion of the media which make for the vascularization of the clot. The changes in the media terminate before the end of the clot is reached, so that some of the thrombus lies in apparently healthy vessel. Here we gain the impression that all the lesions are dependent upon the thrombus formation, and are present for the purposes of organization. In the second variety, however, the same thrombosis is accompanied by more intense infiltration of the media and more active peri-arteritis. In such places it would appear that the same determining cause which leads to the thrombosis also evokes the changes in the media, adventitia, and perivascular connective tissue.

We must not forget the influence of static factors. Indeed the slowing of the circulation alone is a very important agent in the production of thrombosis, and it is rather significant that we so often encounter this disease in the lower extremities and that in all but one of our cases the disease began on the left side where venous stasis is more marked. Doubtless, then, a number of agents are at work in the production of the occlusion. Whatever may be the cause of the thrombosis, we feel inclined to take the view that, although the mechanical conditions that obtain in the lower extremities and the arteriosclerotic changes may be factors, some additional agent, be it toxic or otherwise, is at the same time responsible for the production of the peri-arteritis and thrombosis.

Viewing the process from the standpoint of the pathological lesions, and considering certain facts obtained by clinical observation, it would seem most plausible to assume that certain territories of either the arteries or the veins become rather suddenly thrombosed, in a fashion similar to the thrombotic process that occurs in the superficial veins of the lower extremities. Thus, at one time the dorsalis hallucis and dorsalis pedis, or perhaps plantar arteries or veins, could become closed by red clot; and then the process of organization would take place. Perhaps after an interval of weeks or months a similar process would cause extension upward, or

affect other arteries and veins, until, after a lapse of many months, or a year or more, practically all the larger vessels would become occluded. It is from a study of the age of the process in the various territories that we are led to this supposition. Here too as in the superficial thromboses there is more tendency for the larger vessels to be involved than for the very fine ones; and although the process seems to ascend, it probably does not originate in the capillaries or smallest arterioles, but begins in branches of moderate size. The attendant peri-arteritis could be regarded as being either secondary, or possibly, as being produced by the same causes that lead to the thrombosis. Certain it is that the peri-arteritis is intimately linked with the presence of occluding masses.

Taking the true nature of the lesion into consideration, I would suggest that the names "*endarteritis obliterans*" and "*arteriosclerotic gangrene*" be discarded in this connection, and that we adopt the terms "*obliterating thrombo-angiitis*" of the lower extremities when we wish to speak of the disease under discussion.

I wish to express my indebtedness to Dr. F. S. Mandlebaum, director of the pathological department of the Mt. Sinai Hospital, for the preparation of the photomicrographs which I have shown to elucidate certain points in my paper; I wish to thank Drs. Lilienthal, Gerster, and Sachs for giving me the opportunity of studying their cases, and to acknowledge with pleasure the valuable assistance rendered me by Miss Adèle Oppenheimer and Dr. Mark Cohn, volunteer assistants in the pathological laboratory of the Mt. Sinai Hospital.

ADDENDUM. Since writing this paper I have examined the vessels of eight additional cases of this disease, and have found still further corroboration of what has been said. In one of the extremities a little more than one-third of the anterior tibial was occluded by fairly red recent thrombotic masses; the uppermost portion of the vessel was patent, the distal end as well as the dorsalis pedis and hallucis being occluded by old canalized connective tissue. In another case, the occlusion was old in all of the distal parts of the arteries, recent in the upper part of the posterior tibial and popliteal arteries. The thrombotic process terminated abruptly at about the middle of the popliteal, and could also be traced into the origin of the anterior tibial, where its rounded organized end was found lying 1 cm. below the foramen in the interosseous membrane. The upper end of the occluding tissue that had ascended from the dorsalis hallucis was situated two inches above the ankle-joint, the intervening portion of the anterior tibial artery being patent.

**THE PROLONGED USE AND TOXIC ACTION OF SULPHONAL.**

BY JAMES E. TALLEY, M.D.,

DIRECTOR OF THE CLINICAL LABORATORY OF THE PRESBYTERIAN HOSPITAL, PHILADELPHIA.

ABOUT twelve years ago, a woman then just past middle life, was operated on for uterine fibroids. She had developed a mild melancholic state with insomnia, and was given sulphonal for sleep. A year and a half later, when I first saw her, she had largely recovered from her depression, but still found it necessary to take from 10 to 15 grains of sulphonal every night, or else remain wakeful. The dangers of such prolonged use were pointed out to her then and many times since, but any attempt even to change to another hypnotic always ended in a return to the sulphonal. In the words of the patient, "the number of nights missed in taking sulphonal during all these years is not greater than the number of the years." Formerly she had often to take as much as 15 or 20 grains, but for the last four or five years she has taken 10 grains regularly. Finding that there was little chance of ever getting her to make a determined effort to get rid of a habit which she looked upon as rather necessary, and comparatively harmless, matters were left to drift. I saw her from time to time for minor ills. I examined the urine occasionally and found it normal until about five years ago, when it first showed a trace of albumin and hyaline casts. This condition still persists, but shows no increase, and is not an uncommon condition at her time of life. Repeated examinations of the patient show only that she has the stamp of chronic invalidism, with recurring mild attacks of melancholy. The abuse of the drug appeared to affect her so little as to suggest substitution, but that theory is untenable, since the husband has means of procuring the drug in original packages. That the dosage was correct was proved by furnishing him with accurately weighed pieces of tin foil with which to test his scales. This woman has taken on the average yearly at least a half pound avoirdupois of sulphonal for twelve years, or five and a half pounds in all, and suffered no ill consequences so far.

In November, 1907, the patient was admitted to the Presbyterian Hospital for insomnia and mental depression. She had been taking sulphonal fairly regularly, and was kept on a nightly dose of 20 grains during a short time while we sought to investigate two points: First, although the urine did not suggest hematoporphyrinuria, if the theory of Stokvis is tenable, namely, that the hematoporphyrin of the urine is due to hemorrhage into the intestinal mucosa and the transformation of the hemoglobin there into hematoporphyrin which is absorbed and excreted in the urine, we thought that the stools might give a positive reaction for occult blood. The patient was put on a milk diet and the stools tested, but with negative result.

Again, knowing that traces of hematorporphyrin are found in normal urine, we thought that after this prolonged use of sulphonal we might find at least small amounts present. With the coöperation of Dr. Sydney Repplier and Dr. D. W. Fetterolf, demonstrator of chemistry in the University of Pennsylvania, first the method of Salkowski and then that of Riva and Zoja were tried with negative results. Following this Dr. Fetterolf carried out the more accurate method of Garrod with two specimens of urine taken at intervals of three days; still with negative results. The only reason that can be assigned for the entirely negative results with the Garrod method was the fact that only 200 c.c. of urine was sent to Dr. Fetterolf each time instead of 1000 to 1500 c.c. as desired. Further experiments were impossible, because the patient left the hospital. It is reasonable to suppose, however, that the urine did not contain a large amount of hematorporphyrin when the comparatively sensitive method of Garrod failed entirely to give a positive reaction with even 200 c.c. of urine.

Considering the time that sulphonal has been in use, and the frequency of its use, especially in asylum practice, the number of cases of poisoning by it are comparatively few. However, the cases of poisoning reported are sufficiently numerous to make us cautious in dosage, and especially in the length of time of exhibition of the drug.

Dr. Hunt has found references to at least 50 cases in the literature without making an exhaustive research. Garrod and Hopkins<sup>1</sup> report the case of an epileptic woman, aged fifty years, who had taken almost continually 20 to 40 grains of sulphonal for six years before she developed symptoms of poisoning. The attack proved fatal. The other cases described show varying degrees of susceptibility. Occasionally, idiosyncrasies toward the drug may appear. The man reported by Murphy<sup>2</sup> had taken a single dose of 10 grains on three separate occasions at long intervals, and had suffered each time with itching, swelling of the hands and feet, and a general erythema with vesicular eruptions.

Among the cases of acute poisoning with recovery, Tresilion's<sup>3</sup> case took only 20 grains one night and 15 grains the succeeding night; Hearder's<sup>4</sup> case, 15 grains on each of four succeeding days; Gillett's<sup>5</sup> case 1 dram in four hours; Richmond's<sup>6</sup> case, 2 drams at one dose; and Hill<sup>7</sup> reports the case of a child, aged eighteen months, who received 34 grains in a few hours. Among the fatal cases Pettitt<sup>8</sup> reports that of an insane woman who succumbed to poisoning by 30 grains given in two doses about one hour apart. Schulz<sup>9</sup> records

<sup>1</sup> Jour. Path. and Bact., 1895 to 1896.

<sup>2</sup> Brit. Med. Jour., 1899, 209.

<sup>3</sup> Brit. Med. Jour., 1898, ii, 808.

<sup>4</sup> Med. Record, 1894, xlvi, 339.

<sup>5</sup> Neurol. Centralbl., October, 1896.

<sup>6</sup> Indian Med. Gaz., 1904, xxxix, 96.

<sup>7</sup> Lancet, 1896, ii, 1372.

<sup>8</sup> Ibid., 1337.

<sup>9</sup> Med. News, 1889, lx, 165.

that an hysterical woman died from the effects of one-half ounce given during the course of a month. Other cases vary in time from weeks to months of fairly constant use of average doses before the development of symptoms of poisoning which proved fatal.

The symptoms are pretty uniform in all the well-developed cases of poisoning. They consist in epigastric pain, nausea, vomiting, acetone odor to the breath, usually constipation, low temperature, shallow respiration, feeble pulse, cyanosis, scanty dark reddish urine due to hematoporphyrin, which may or may not contain albumin, casts, degenerated blood corpuscles, and much urobilin; ataxia, delirium, or stupor, and gradual development of motor and sensory paralysis, and finally death, usually from respiratory, sometimes from cardiac arrest. Some autopsies have been reported, but few, if any, cases have been so exhaustively studied, both clinically and pathologically, as the case reported by Taylor and Sailer.<sup>10</sup>

A point in prognosis is the observation that all the cases that have recovered have had some or all of the gastro-intestinal, nephritic, respiratory, and circulatory symptoms, but no nervous symptoms beyond stupor and ataxia. The development of paresis appears always to run on to complete paralysis and death.

The predominance of constipation among the toxic cases, should put one on the alert to keep the bowels active during the exhibition of the drug, but that free purgation is not able to eliminate the poison when once absorbed and the mischief begun is shown in the first case reported by Smith. The woman had diarrhoea the greater part of the twelve days between the first signs of poisoning and death.

The conclusions are that, although the patient the subject of this report has taken perhaps an unprecedented amount without any symptoms of poisoning so far, the prolonged use of sulphonal is never a safe procedure, as the literature attests. The appearance of even the first symptoms of poisoning is apt to be the beginning of a condition over which we have no control. It is safer, therefore, occasionally to discontinue its use, changing for a time to other of the hypnotics, if the necessity of the case demands their constant use.

<sup>10</sup> William Pepper Clinical Laboratory Reports.

## REVIEWS.

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**HEREDITY.** By J. ARTHUR THOMPSON, Regius Professor of Natural History in the University of Aberdeen. Pp. 605; 49 illustrations. New York: G. P. Putnam's Sons; London: John Murray, 1908.

SOMEONE has compared the boasted knowledge of science, when thought of in relation to that which is unknown in the realm of nature, to a few scattered and badly torn and blurred pages of some missing but magnificent volume. If one would worse confound his friend who believes only that which he sees, let him direct him into the labyrinth of heredity—that friend whose pedantic materialism denies life when intelligent corporeal existence ceases; for he cannot declare the beginning or deny the existence of its germ, and his assertions only force it back and back into the infinity of the unknown. Professor Thompson, in his preface, almost complains of the vastness of literature which has accumulated from work upon the subject. His book is in the highest degree scientific, logical, and critical; but in the end he unhesitatingly justifies the failure even to approach the final solution of the problem of inheritance by reminding us that there is something more than the mere material inheritance, that we are dealing not merely with things, but with living things. The book is comprehensive and aims to give in as simple a manner as possible a just, conspectus of the facts and theories of inheritance; but, sparkling with epigrams, well written in crisp English, patiently and judiciously paragraphed, insistent by its repetitions and parallelisms, it is in the nature of things not simple and requires careful reading.

The first chapter is devoted to a statement of the problem of inheritance and to an endeavor to define strictly the terminology. In the chapter on the physical basis of heredity the general idea of germinal continuity is developed; a distinction urged between the modes of division of unicellular organisms and the reproduction of multicellular individuals; the distinction drawn between the somatic cells of the latter and the germ cells; a description given of the phenomena of maturation and amphimixis; and in outlining development the conclusion is tentatively drawn that the actual material transmitted has been chromatic nuclear substance. At the same time, resting upon the work of Delage, Loeb, and others, the author is careful to urge that we be "chary in unreservedly committing our-

selves to the idea that the heritable organization resides exclusively in the chromatin of the nuclei of the germ cells." A work of much value in this connection, which the author has evidently failed to meet, is that of Conklin upon the organization and cell-lineage of the ascidian egg (*Jour. Acad. Nat. Sci. of Phila.*, 1905, vol. xiii, Part 1) in which the latter author has shown a very definite substance differentiation in the cytoplasm of the unfertilized ovum foreshadowing (as clearly followed by Conklin) the cellular differentiation of the developing embryo after fertilization. However, Conklin shows that this ovocytic organization is not primordial, and that at least in some important parts it is dependent upon nuclear influence and contribution.

In the third chapter, on heredity and variation, is developed the modern idea of evolution by marked variations or mutations, suddenly appearing upon a given stock and happening to find suitable environment for persistence (De Vries); not by gradual adaptation to conditions of environment with the elimination of the unfit as the old Darwinian theory contemplates. In the fourth and fifth chapters the subjects of blended inheritance, exclusive and particulate inheritance, and reversion and allied phenomena are treated of. The question of telegony is dealt with at some length; as may be supposed, the author is utterly unwilling to subscribe to a belief in the influence implied—it stands with him as "non-proven." In the same way in the brief consideration of maternal impressions he is "scientifically skeptical and gives a verdict 'non-proven' without dogmatically saying 'impossible,'"—a position which, if anything, is a recession from the absolute denial which has been common for years. For medical men (although the whole book should be read, unless the reader be familiar with the details of the subject) the chapters on the question of transmission of acquired characters and upon heredity and disease are of especial interest. Acquired modifications, in the sense of the old Lamarck theory of selection evolution, are practically ruled out by the author, who admits even Brown-Séquard's epileptic mice only in the sense that perhaps a toxin developed in the parents may have influenced the germ cells or the foetus in such a manner that the latter subsequently became epileptic. Modifications of the germ cell by nurture, altering its condition and thus inducing fault in the offspring (nurture here including all nutritional, thermic, or toxic conditions), are accepted; but definite mutilations or structural changes "induced by a change in environment or in function and persisting after the factors inducing it have ceased to operate," these the author does not accept, because he does not find evidence of their occurrence. But he holds it unscientific to deny absolutely their possibility. He clearly points out the impossibility of an inheritance of an infectious disease: the germ cells are not tuberculous; the foetus may antenatally become infected with tuberculosis, but this is not inheri-

tance; it is infection, just as truly as is the postnatal acquirement of the disease. That an infectious disease of the parent can influence the offspring is not denied. It may kill the germ-cell before or after amphimixis; it may deteriorate it and thus influence seriously the offspring; it may attack the foetus in its development and leave any one of a variety of effects upon it; the immunity which a mother acquires may, through the placental connection, come to the offspring. True heredity involves structural and functional elements; these, in the accepted sense of what disease is, may be rare, but are real and may also involve predispositions toward disease. In the strict sense heredity and disease are to be thought of in the same way as heredity and acquired characters; confusion of the real point in transmission and lack of clarity of verbiage must account for the common but fortunately decreasing reliance among the medical profession upon heredity for an explanation of a great variety of disease manifestations.

The chapters on statistical study of inheritance, dealing with Galton's law of ancestral inheritance and of filial regression (tendency of offspring to return in given characteristics to the average of the stock), with the experimental study of inheritance (in which the discoveries of Mendel and his theory of gametic segregation are discussed), and the bearing of consanguinity of parent organisms upon the offspring, are clear expositions of the real work of discovery in the field of inheritance; and that they are not in perfect harmony and do not lead to a final and satisfactory conclusion is no fault of the book or its writer—it is due to the vastness of the field, the multiplicity of the factors engaged, and finally, to the fact that the element of vitality, whatever that may be, enters in a dominant but utterly unknown manner. Then follow chapters upon the theories of heredity, the old theological or spiritual theories, the metaphysical theories of *fetus in primordio in potentia*, and the preformationist theories (*homunculus in homunculo*), the various theories of pangenesis (Spencer, Darwin, Jaeger, Galton, Brooks), and that of germinal continuity (Owen, Haeckel, Jaeger, Brooks, Galton, Nussbaum, Weismann); upon development (Weismann's theory of germ-plasm and germinal selection more particularly); upon heredity and sex determination (in which the author clearly regards sex as transmitted dually with domination of one or other in the offspring, but is unable to add in the least to the solution of the problem why such dominance takes place); and upon the social aspects of the studies upon heredity and evolution for man. A valuable representative bibliography, with an excellent additional index of the bibliography (indicating the most important works bearing upon the different phases of the subject), and a general index to the text of the volume occupy the remainder of the pages.

Such a book is not subject to criticism in the ordinary meaning; it is to be commended. It is a summary of a vast amount of labor



which has been carried out by an army of students, and is presented with no more bias than the present position of general scientific studies requires. The reviewer sits at the feet of these students, and is grateful to the author for the work he has ungrudgingly and consistently given to the preparation of such a conspectus. The pity is that there is so much to be known; that there is so much that is vital to our conceptions that is apparently unknowable. The one link which would most help now to the clarification of much that is clearly in the realm of the knowable, concerns the relation between the division of the unicellular organism and the multiplication of the multicellulars. That there is such a connection can scarcely be doubted, even though at present the two processes seem so isolated. From it would rapidly come some clear appreciation of the moot point of transmission of acquired characteristics, and the whole subject of evolution would be illuminated. The reviewer believes that Conklin's contribution on the nuclear and cytoplasmic relations of the germ cell and the preformation of the organism in the ovocyte bears with no little weight in this direction, and promises much in the future elaboration of our ideas. Principles must permeate the whole scheme of gametic history; cell cleavage holds for both unicellular and for multicellular propagation; and the question is, What is the preparation, quantitative and qualitative, which precedes cleavage, and how does such preparation favor cell differentiation in the multicellular? Are all of our somatic cells duplications of the fertilized maternal cell, with special growths of one character, but without destruction of all else? Or are all these cells *sui generis* because in the ovocyte there was segregation of special characteristics to special parts of the ovum before development was excited or permitted by fertilization? There are academic and at the same time practical reasons for believing both ideas are true; they are not mutually subversive. And much of the mode of action depends upon that vital character which is intangible in itself but is manifest clearly in its result of specific identity in the realm of created things. Conklin makes out differentiation in his ascidian egg by the fact of variation in color of different parts in the living egg; but differentiation need not involve color; and in another species with even higher differentiation this index may not exist. Nor does differentiation depend on size; but diminished size materially adds to the difficulty of observation. Grant that there is such germinal preparation, simple or complex as the specific position of the organism demands, and much of the further difficulty is lessened. This would open the way to appreciation of the influence of a variety of potentialities of the environment; and Galton's ancestral law and Mendel's phenomenon and Weismann's determinants all would find no difficult appreciation.

A. J. S.

THE COMMON SENSE OF THE MILK QUESTION. By JOHN SPARGO. Pp. 351; 26 illustrations. New York: Macmillan & Co., 1908.

THE author undertakes in the present volume to consider the milk question from every possible standpoint. He takes up the question of the protection of the infant and lays some stress upon the tendency to race suicide; he considers the importance of maternal nursing and discusses the causes of the well-known fact that maternal nursing is becoming more difficult, especially among the fortunately situated mothers; he discusses the possible substitutes for mothers' milk, pointing out the reasons for the almost universal use of cows' milk, after which he very effectively illustrates the filthy conditions under which cows' milk is produced, and discusses the milk-borne diseases; he points out the relative merits of pure milk and pasteurized milk; and he outlines a policy of reform in the production of milk.

The descriptions of the conditions under which the ordinary market milks are produced are accurate and lucid and, if widely read, ought to contribute much toward educating the public to the need of reform in the methods of milk production. The illustrations strengthen the value of the book in this regard, inasmuch as they give very striking pictures of the filthy conditions under which milk is produced, contrasted with the production of milk under conditions of cleanliness.

The chief point on which the reviewer would take issue with the author relates to his advocacy of municipal pasteurization of milk. It must be admitted that there are two sides to this very important question. Up to the present the majority seem to be opposed to the municipal pasteurization of milk; naturally, those who are most bitterly opposed to this process are the members of the medical profession, who are especially devoting themselves to the study and treatment of the diseases of early life. There is probably no class of individuals who are more thoroughly conversant with the distressing conditions of the market milk and its disturbing effects. Their attitude, therefore, is very significant. One who studies the milk question from a layman's standpoint, as the author of this work has done, can naturally see but one side of the question. He attempts to be fair in the discussion of the two sides, but it is rather difficult to follow the reasoning which leads him to the deductions which he makes.

All of those who are opposed to the municipal pasteurization of milk admit the advisability of pasteurizing the ordinary market milks, but they believe this can be more satisfactorily done in the home of the consumer than by the dealer. The opposition to pasteurization is based on the belief that pasteurization must necessarily lead to carelessness on the part of the producers, who have the feeling that it matters not what the nature of a product is, the consumer

is protected from the injurious effects of the defective milk by the process of pasteurization. Furthermore, the pasteurization of milk would have the effect of making legislation more difficult. Under existing conditions, the accomplishment of legislation directed toward improving conditions at the source of supply and in the subsequent handling of the milk is very difficult.

If he of political mind is to be comforted by the belief that protection against injury can be accomplished by pasteurization, he is naturally going to be still more lax in his efforts to bring about improvements at the source of supply. One of the most important arguments against pasteurization, and one upon which the author lays little stress, is the danger of commercially pasteurized milk. Even under the best conditions, including the Strauss laboratories, which represent the method recommended by the author, complete pasteurization of the milk is rarely accomplished. The pasteurization of milk disturbs the property which all uncooked milk possesses—of protecting itself to some extent against the development of the microorganisms which it contains. If, therefore, these partially pasteurized milks are not properly kept, they are likely to become a source of danger to the consumer. Where pasteurization is done on a wholesale basis, the possibility of re-infection of the milk is greatly enhanced, and it is very questionable if, in the end, there could be brought about any reduction in the infant mortality by its use. As the author points out, pasteurization is a makeshift at best. When properly done, it has no cleansing effect upon the milk; the manure and other filth which gets into it are not removed.

The reviewer holds the opinion, which is shared by many, that the accomplishment of a satisfactory system of pasteurization of the milk supply would entail almost as much effort as a systematic crusade by the city authorities and the medical profession against the present methods of defective production. We would have been more pleased had the author advocated the establishment by the city authorities of laboratories for the distribution of a modified milk of pure quality. It is entirely possible so to re-organize the working methods at many of the points of production, without great expense to the producer, as to yield a product which could be used safely without pasteurization.

If the medical profession and interested laymen in the various cities in the country would make the same united effort to bring about this improved condition as those interested in the crusade against tuberculosis have done; if they should adopt the same system of education by frequently repeated exhibitions of the filthy conditions under which milk is produced, we are of the belief that legislation could be accomplished that would so much improve the production of milk that it could be safely used without being pasteurized.

We sincerely trust that this book will be widely read by the

laity and the medical profession, because it will educate them to a knowledge of existing facts in a more satisfactory manner than any work with which we are conversant, but in reading it, we trust they may not be influenced to favor municipal pasteurization instead of improvement at the source of production. S. M. H.

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**PROGRESSIVE MEDICINE.** A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College. Assisted by H. R. M. LANDIS, M.D., Demonstrator of Clinical Medicine in the Jefferson Medical College, Philadelphia. Volume III, September, 1908. Philadelphia and New York: Lea and Febiger, 1908.

VOLUME III of *Progressive Medicine* opens with a discussion of recent advances in diseases of the thorax and its viscera, including the heart, lungs, and bloodvessels, comprising 100 pages, by William Ewart. It includes such important subjects as tuberculosis in its varying aspects, physical examination of the chest, bronchitis and other bronchial affections, pleuropneumonia, pulmonary complications following anesthesia, acute suffocative catarrh of Laennec, emphysema, vicious circles associated with disorders of the heart, functional disorders of the heart, valvular diseases, the treatment of heart disease, arteriosclerosis, the blood pressure in relation to disease, etc. William S. Gottheil devotes 44 pages to dermatology and syphilis, discussing, among other subjects, actinomycosis, blastomycosis and coccidioidal dermatitis, general dermatological diagnosis, drug eruptions, lupus, negro skin diseases, tuberculosis of the skin and the tuberculin test, the x-rays in dermatology, and the many aspects of syphilis. Edward P. Davis devotes 100 pages to obstetrics, discussing especially changes in the various organs during pregnancy, pyelitis, pregnancy complicated by disease of the pelvic viscera, and by heart disease and tuberculosis, chorio-epithelioma, eclampsia, ectopic gestation, labor and its complications, the surgical management of the puerperal period, puerperal septic infection, etc. William G. Spiller devotes 41 pages to diseases of the nervous system, particularly brain tumor, aphasia, arteriosclerosis, hemiplegia, paresis, cerebral localization, tabes dorsalis, poliomyelitis, and various disorders of the peripheral nerves. As a whole the volume is of unusual interest and merit—a virtual necessity in these days of rapid progress.

A. K.

STATE BOARD QUESTIONS AND ANSWERS. By R. MAX GOEPP, M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic and College for Graduates in Medicine. Pp. 684. Philadelphia and London: W. B. Saunders Co., 1908.

THE exigencies of the situation in which the recent graduate in medicine finds himself when, having gone forth with a sheepskin and a blessing from his Alma Mater, he desires to undertake the practice of medicine, and the much more serious situation in which the established practitioner finds himself when he desires to remove to another State, furnish at least the reason for a book such as Dr. Goepf has prepared, with the assistance of Drs. W. R. Nicholson, D. W. Fetterolf, and G. M. Dorrance. The one essential is that the unfortunate doctor should be able to answer satisfactorily about 70 per cent. of a series of questions on the different branches of medicine. That which assists in the satisfying of this condition should be commended. Perhaps, in the majority of cases, the sort of State examinations at present in vogue, though pregnant with obvious and serious faults, fulfils most of the desirable requirements; and in the absence of any better test of fitness to practise medicine, Dr. Goepf's book (and others of its kind) may be described as "filling a long-felt want." It is stated in the preface that the questions contained within the volume were selected from the many asked at State Board examinations during the last four years, preference being given to those asked in the larger and more representative States (witness the soft impeachment!); as Dr. Goepf states, that may, therefore, be regarded as fairly representative of the kind of examination questions usually propounded by State Boards, but he hastens to add (as a veiled indictment of some one?) that many questions were rejected because they were unsuitable in content or in wording, and he is not certain that the questions finally selected and embodied in the book are all above criticism. This, however, cannot be construed as a defect of the book, but of the material upon which the book had to be built.

The volume is made up of a large number of questions and answers on physics, chemistry, physiology, anatomy, hygiene, materia medica, practice of medicine, surgery, obstetrics, gynecology, pathology, and bacteriology; these to a considerable extent have been arranged in a manner that may be described as proceeding from the simple to the complex. A more than cursory examination of the book shows the answers to be clear, concise, accurate, and sufficiently explicit for the purpose in mind. The information has been taken freely from standard text-books, with no attempt to indicate the sources, since no originality is claimed; this is really the only noteworthy defect of the volume, the value of which would have been much enhanced had the authors of at least the most important definitions and descriptions been mentioned, as has been done in at

least one other similar book; perhaps, however, this is only a personal view of the matter. The evident care with which the volume has been prepared and the avidity, doubtless, with which it will be read by those in serious need of cramming, furnish mute testimony of the serious defects in the State examinations, among which may be mentioned, the absence of provision to test the practical knowledge and ability of the examinee; the non-allowance of credit for consistent satisfactory work done throughout the college course in medicine; the inclusion of questions on matter long since forgotten and of little practical or other value to the physician; no credit for years of exemplary practice, except in the comparatively few reciprocating States; and no special provision for the specialist, etc. Until such time as a more equitable method of conducting State examinations is devised, books such as Dr. Goepf's will prove of distinct value and assistance. Dr. Goepf's book itself excellently fulfils the purpose intended; it may be read with profit not only by those under the necessity of appearing for State examinations, but also by others desiring concise information on the topics of which it treats.

A. K.

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**TEXT-BOOK OF OPHTHALMOLOGY.** By DR. ERNST FUCHS, Professor of Ophthalmology in the University of Vienna. Authorized Translation from the Eleventh Revised and Greatly Enlarged German Edition, with Numerous Additions by ALEXANDER DUANE, M.D., Surgeon to the Ophthalmic and Aural Institute, New York. Third edition; pp. 908; 441 illustrations. Philadelphia and London: J. B. Lippincott Co., 1908.

THE reception accorded to the previous editions of this work the world over is the best testimonial of the consideration it enjoys in the opinions of those who are interested in the subject with which it deals. A work like this has one undoubted advantage over encyclopedias, in being the product of a single mind. The various subjects dovetail into each other more intimately, and the whole leaves a smoother and more uniform impression than when the different parts are the work of different men.

This book states the facts of ophthalmology plainly, so that they can be understood by any medical reader. There are no abstruse discussions such as are sometimes found in works by German writers. More space is given to the important subject of refraction than in previous editions, though it still remains true of this, as of the others, that it is most successful in its treatment of the affections of the anterior segment of the eyeball. In a preface to an early edition the author justifies this on the ground that diseases of the deeper structures offer a field for the triumph of diagnosis,

but nothing more. It is satisfactory to think that the last decade has made a change in this respect, and that the early recognition and treatment of affections of the fundus by subconjunctival injections can now also celebrate its triumphs.

When we turn to what may be termed the controversial departments of ophthalmology, such as the removal of the lens in high myopia, and the alleged reflex influence of refractive and muscular errors, the note is eminently conservative. Fukala's operation, for example, is recommended for young persons whose myopia amounts to more than 15 D, and who do not show excessive pathological changes in the fundus. We are reminded, however, that the operation will not check the increasing elongation and changes in the fundus. We find no mention of the grave reflexes alleged by some writers to be due to ocular disturbances.

It is hardly necessary to state that the book has been brought up to date as regards late views in all the departments of ophthalmology, a good portion of which is from the pen of the translator, the latter applying especially to those departments which may be termed American.

Finally, an estimate of the work would be incomplete without special mention of the part taken therein by Dr. Duane. The old saw, "*traditore i tradutore*," is brilliantly refuted in this translation. Familiar as we are with the German work, we do not hesitate to say that the English edition is superior to the original, for not only is the latter in all respects the equal of the former, but the amount of new matter which has been most judiciously incorporated by the American editor has undoubtedly made the book distinctly more valuable, so that this edition is unhesitatingly to be recommended even to those readers who are well enough acquainted with German to read the work in the original.

T. B. S.

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DISEASES OF THE NOSE, THROAT, AND EAR. By WILLIAM LINCOLN BALLENGER, M.D., Professor of Otology, Rhinology, and Laryngology in the College of Physicians and Surgeons, Department of Medicine of the University of Illinois. Pp. 904; 471 engravings and 16 plates. Philadelphia and New York: Lea & Febiger, 1908.

In this book the author has aimed to cover the entire field of rhinology, laryngology, and otology in such a manner as to give to each subject its adequate importance instead of, as he states is usually done, "dealing fully with the nose and throat and only with the associated affections of the ear." In the accomplishment of this aim, Dr. Ballenger has been most successful. The chief characteristic of his book is the thoroughness with which the practical aspects

of the subjects considered are represented. It bears witness on every page to its author's work as a teacher and of his vast clinical experience. Dr. Ballenger, as is well known, has been among the foremost in this country in the perfection of the operation for the submucous resection of the nasal septum. He has also done much toward the elaboration of the proper technique for the extirpation of the faucial tonsils. Both of these procedures are dealt with in masterly fashion and a most adequate description given of the chief methods for their performance. The directions for the performance of the major operations of aural surgery are most excellent. A perusal of his book shows the originality of his mind and the thoroughness of his knowledge of the anatomy and pathology of his subject.

Dr. Ballenger's book can be highly recommended as a real contribution to otological literature, not only as a text-book, but as a work of reference for the specialist. There are a few curious errors in the computation of the strengths of the solutions to be kept in the laryngologist's office. Thus the statement is made that one-half dram of nitrate of silver to the ounce of distilled water is equal to a 12.5 per cent. solution. Otherwise, the text is singularly free from error. The book is copiously illustrated, the pictures, a large majority of which are original, being well reproduced. F. R. P.

**A TEXT-BOOK OF DISEASES OF THE NOSE AND THROAT.** By D. BRADEN KYLE, A.M., M.D., Professor of Laryngology and Rhinology in the Jefferson Medical College, Philadelphia. Fourth edition; pp. 725; 215 illustrations, 26 of them in colors. Philadelphia and London: W. B. Saunders Co., 1907.

THE success of Dr. Kyle's book is sufficiently well indicated by the fact that four editions have been called for within the few years that have elapsed since its publication. The present edition has been thoroughly revised and the book considerably enlarged. All of the most recent advances in rhinology and laryngology are considered. The work is adapted not only to the student and general practitioner who wishes to have a safe guide to the study of the subjects contained in it, but, owing to its author's profound knowledge of pathology and anatomy, he presents more of the philosophy and underlying principles of laryngology and rhinology than is ordinarily found in works dealing with them. An excellent description of tracheoscopy and bronchoscopy has been added to the book since the last edition. F. R. P.



# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**Fatal Asystole in Exophthalmic Goitre.**—G. MORIQUAND AND L. BOUCHAT (*Semaine médicale*, 1908, xxviii, 325) have analyzed 260 cases of exophthalmic goitre, to determine whether the fatal asystole occurring in some cases may be due to the tachycardia or not. In many cases it was found, on closer examination into the histories, that a previous more or less severe cardiac disturbance had been present; this was the case in a patient who developed exophthalmic goitre during convalescence from an attack of acute articular rheumatism, and who died in a couple of months from cardiac weakness. On more careful examination into the history of this patient, and pathologically of the heart itself, it was found that the apparently fatal outcome of the exophthalmic goitre had in reality been due to a previous pericardial and myocardial involvement. The same was found true in the majority of the cases from the literature: that the fatal cardiac event was the result of an aggravation, due to the tachycardia, of a preëxisting cardiac disease.

In a second group Moriquand and Bouchat have considered those cases in which the heart (not examined histologically) was considered sound, and the fatal asystole due to some other underlying cause, as Bright's disease, severe pleurisy, or mediastinal compression. In the last group there seems to be no other cause but the tachycardia (in these cases the histological examination of the heart is most important), the course of the disease is downward and rapidly fatal, the heart weakness being manifest a few weeks after the first symptom due to the goitre are seen. It is often possible in this group of cases to trace to some infection, generally recent, the thyroid and the cardiac lesion, the association of which furnishes the two causes most favorable for a fatal cardiac breakdown—tachycardia and an inflammatory process.

**Some Mechanical Factors in the Production of Lymphocytosis.**—F. PEYTON ROUS (*Jour. Exper. Med.*, 1908, x, 238) concludes, from his study of the subject, that the lymph of the thoracic duct furnishes to the blood a larger proportion than is usually supposed of the lymphocytes in the circulation, and this must affect very considerably the blood picture, when gross variations in the output of the duct may be brought about by mechanical factors (pressure). Rous found that the quantity of lymphocytes supplied through the thoracic duct remains practically unchanged under normal conditions, therefore the tissues producing lymphocytes are "set" at a rate of activity, definite in each individual. Muscular activity (dog's struggles) was found to produce a prompt increase in the output of lymphocytes through the duct; they increased in numbers with continued exertion and showed a slight fall in number for a short time after a prolonged struggle. The use of a lymphagogue (glucose) brought about the same general results. This factor of the muscular activity, with its effect on the flow of lymph from the thoracic duct and increase in the number of lymphocytes is of special interest when considered in relation to the following article on the "Blood in Pertussis," as the mechanical factor of strain and struggle in the coughing child must cause some change in the output of the thoracic duct, due to the change in pressure within the thorax and lungs during the paroxysms.

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**Morphology of the Blood in Pertussis.**—JOSEPH H. BARACH (*Archiv. Int. Med.*, 1908, i, 602) gives a careful study of the blood in 50 cases of whooping cough, and finds that there is present at first a leukocytosis, with an increase of all the cell forms; then follows a small cell lymphocytosis, which continues to increase together with the large lymphocytes, though the other cells have reached their limit in numbers. Later, with the fall in leukocytosis, which is by lysis, mast cells and occasionally myelocytes, are often seen; and during this lysis an eosinophilia is noted for a variable time, with a gradual return of all elements to the normal. In the first half of the blood cycle there then is a lymphocytosis, and in the second half a relative increase in the polynuclears and a decided eosinophilia. Clinically the leukocytosis begins with the first coughing; this increases and the lymphocytosis becomes marked. The height of the leukocytosis (22,000 average in 50 cases) is reached in the spasmodic stage and depends on the severity of the attack. When the improvement is beginning the leukocytosis has decreased, but the polynuclears have relatively increased and the eosinophilia is present. Barach has found the blood examination of value in the early diagnosis, and of distinct advantage in negative as well as positive cases.

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**The Occurrence of Bacillus Typhosus in the Blood of Non-typhoid Patients.**—BUASE (*Münch. med. Woch.*, 1908, lv, 1113) reports four cases in which *Bacillus typhosus* was isolated from the blood of patients who were not ill with typhoid fever. In all the cases the Widal reaction was negative. Two cases were diagnosticated typhoid because of the bacilli in the blood, but at autopsy proved to be a miliary tuberculosis of various organs, including the intestines. In a third case, while

the patient was under observation, symptoms of an abdominal disorder, with diarrhoea, pain, etc., appeared. At autopsy this proved to be a disseminated tuberculosis. The fourth case was one of acute pneumonia with diarrhoea. The patient recovered. Buase is certain that there could have been no mixing of specimens, and that the bacilli were *Bacillus typhosus*. He believes that many persons carry *Bacillus typhosus* in their intestine, and that possibly only when catarrhal or ulcerative conditions of the intestine give the bacilli opportunity to enter the blood do they develop pathogenicity. He concludes that even the presence of *Bacillus typhosus* in the blood does not furnish absolute proof of the presence of typhoid fever even when a strong suspicion of typhoid exists.

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**Further Researches on Extra-uterine Blood Formation.**—E. MEYER (*Munch. med. Woch.*, 1908, lv, 1161), in a previous paper upon the severe anemias with special reference to pernicious anemia, had pointed out that the liver, spleen, and, at times, lymph glands, all organs which normally in extra-uterine life produce no blood elements, contain in these diseases collections of young lymphocytes and erythroblasts. Further, in the majority of cases there is a proliferation of bone marrow, resulting in a richness in large nucleated red cells and cells which resemble the small non-granular lymphocytes.

Meyer regards these changes as reparatory, and in this paper has tried to reproduce some of them. In animals which were poisoned by pyrogallol or pyrodine and which survived the poisoning one month or longer, Damarus found in both the liver and the spleen groups of young lymphocytes and young nucleated red cells. The anatomical changes noted by Damarus correspond almost completely to those noted in pernicious anemia—lack of granulated cells in the marked proliferated red marrow, hyperplasia of the splenic pulp in twelve small follicles. In the veins of the spleen and the capillaries of the liver there were numerous lymphoid cells and erythroblasts; also some extravascular collections of these cells. The whole picture was much like that seen in the embryo. Butterfield has been able to find in the blood of leukemic persons as well as in the organs and blood of the human embryo, besides typical myelocytes, all transitional forms to the large non-granulated basophilic cells (lymphocytes). Meyer does not believe that we have any right today to differentiate the precursors of the granulated cells from those of the lymphocytes. He considers the main question with which the pathology of the blood is confronted to be that of the mother cell of the small lymphocytes; he holds leukemia to be a disease of a certain form of tissue, not of a single organ, and can see no rational basis for its treatment by splenic removal or "x-rays," nor has he ever noted any practical results from these procedures.

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**Atoxyl in Malaria.**—GOUDE and DORPAS (*Wien. klin. Woch.*, 1908, xxi, 837). Experiments were conducted upon the peasants of a malarial district of the Adriatic. Six cases are reported, three adults and three children. Atoxyl solutions were injected either subcutaneously or intramuscularly into these patients; the blood of each previous to

treatment had shown a great number of parasites. The initial doses for adults was usually 0.04 gram (0.6 grain), and this was followed every second day for four or five treatments by 0.1 gram (1.5 grain). Children received about one-half of these doses.

During treatment, the patients felt much better, because free of fever and in two cases the spleen decreased in size. In only two cases did the parasites disappear from the blood; in all others the tertian gamete form of parasite persisted. These were not killed off by subsequent injections of quinine. Gouder and Dorpas do not believe the atoxyl exerts the lethal effect which quinine does upon the parasites. They are inclined to think that perhaps larger individual doses and longer treatment may effect cure.

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**Absence of the Patellar Reflex in Hysteria.**—G. KÖSTER (*Deut. Arch. f. klin. Med.*, 1908, xc, 3, 4) describes an instance of hysterical astasia and abasia, in which the patellar reflex and the tendo Achillis reflex were absent bilaterally. The muscles of the lower limbs were in a condition of hypotonia. The absence of the reflexes cannot be referred to cutaneous anesthesia, since sensation was not disturbed in the vicinity of the knee. Moreover, cases of complete hysterical anesthesia and paraplegia commonly exhibit the patellar reflex. Nor is hypotonia incompatible with the presence and even exaggeration of the reflex. Not only is such association found in hysteria, but also in morbus Basedowii, in myasthenia, and in chronic CS<sub>2</sub> poisoning. Because of the numerous hysterical stigmata in this case, the clinical diagnosis of hysteria cannot be doubted. Subsequent death (attributed to heart-failure during an epileptic seizure) allowed examination of the brain and medulla, with negative findings. Köster is of the opinion that if attention is once centred on this phenomenon, other cases will soon be added to those already observed of absence of patellar reflex in hysteria.

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## SURGERY.

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**Shortening the Course of Healing by Getting the Patient out of Bed Early.**—KUMMELL (*Archiv f. klin. Chir.*, 1908, lxxxvi, 494) says that for several years he has been getting his patients out of bed as soon as they could stand, after operations for surgical conditions of the upper

extremities, the breasts, neck, and head. In this way convalescence has been made more favorable and more brief. Even old people, almost without exception, have been gotten up for brief intervals in an easy chair for the purpose of avoiding lung complications. Abdominal hernia has not occurred. He has observed in young individuals, especially strong boys, who throw themselves about soon after operation, that the convalescence was shorter and the subjective disturbances less, than in other patients. Intestinal disturbances, particularly, were less disturbing. By getting the patient out of bed early after operation, the tendency to the formation of thrombi and emboli, is decreased, owing to the improvement in the circulation and heart strength brought about by the free movements. He believes that continued rest in bed, especially in corpulent, anemic, and weak patients, is largely responsible for the frequent femoral thromboses and lung emboli. The results of other surgeons in this direction are quoted. Kronig, who got his laparotomy patients out of bed on the first day after operation, in 300 laparotomies, saw no thromboses or emboli, no postoperative pneumonia, ileus, or hernia. Similar results were observed by Hartog, Ries, Chandler, Boldt, etc. Kümmell reports 164 laparotomies in which he got the patients out of bed on the first or in a few days after operation. He observed no thromboses, although one died on the tenth day from pulmonary embolus. This was a very corpulent individual, with a weak heart, operated on for an extensive umbilical hernia. This method of treatment in his cases led to the development of a stronger and thicker cicatrix than the old method. The employment of the catheter is less frequently necessary, and the good effect on breathing reduces the tendency to bronchitis and pneumonia. The use of scopolamin-morphine chloroform or ether anesthesia has probably aided in this direction. In order to aid the patients in getting out of bed early attention to a few conditions is necessary, as: a proper administration of the narcosis, so that vomiting will be avoided; a rapid operation with small loss of blood; a faultless antiseptic course of healing; and firm sutures. For the formation of a firm scar, the kind of suture and suture material is important. The peritoneum and muscles are sutured separately with continuous catgut. The fascia is first freed and then overlapped by a similar suture. Silk is employed for the skin sutures. On the second, at the latest on the third day, the patient is gotten out of bed. When the weather permits he may be permitted to go for a walk outside, and is discharged on the tenth to the fourteenth day.

**Concerning Compression of the Pelvis in Trendelenburg's Operation for Ectopy of the Bladder.**—WILMS (*Deutsch. Ztschr. f. Chir.*, 1908, xciii, 321) says that by Trendelenburg's method of compressing the pelvis, in spite of the greatest care, from the compression of the belt employed, ulceration over the great trochanters and anterior iliac spines can scarcely be avoided. Wilms aims by a specially constructed iron arch, to bring the necessary pressure directly over the bones, even at the risk of a slight necrosis. The weight of the apparatus does not lie on the body of the child. At each end of the arch is a screw guarded by a bolt, so that the degree of pressure can be regulated, and at the end of the screw a wooden block is fixed. Several pointed nails are fitted into holes in the wooden block. These nails are first passed to the pelvic

bones slightly behind the anterior spines. As a preliminary operation the pelvic bones are chiselled through alongside the sacrum, and eight days are allowed for healing of the wound. The nails are introduced to the pelvic bones and the edges of the opening in the bladder are freshened and sutures introduced without tying. The rest of the apparatus is then fitted to the nails and the screws tightened. The bones are easily pressed together, and after close approximation of the bones at the symphysis the sutures are tied. Further sutures are then introduced as they are found necessary. The children do not complain later of pain from the nails, and can be picked up and cleaned. The apparatus should be left on from four to five weeks.

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**The Treatment of Phosphorus Necrosis.**—TELEKY (*Archiv f. klin. Chir.*, 1908, lxxxvi, 369) says that the conservative treatment with incision, irrigation, and drainage of painful abscesses, curetting of sinuses, and extraction of completely separated sequestra, is to be preferred to subperiosteal, partial resection of the lower jaw. The disadvantage of long continued suppuration will be overcome by the advantage of a certain prospect of definite healing by the better cosmetic and functional effect which will be produced by the good and permanent layer of bone left after the removal of the sequestrum. The disadvantage of the early resection lies in the apparent impossibility of determining the limits of the diseased and healthy bone, and in the uncertain, often very deficient or absent regeneration of bone. There is the possibility that by resection and its accompanying irritation of the periosteum, the latent phosphorus intoxication may become manifest in the bone bordering on the resection, and rekindle acute symptoms. The cases of resection of the lower jaw for phosphorus necrosis are not suitable for immediate prosthetic apparatus. From the extending diseased process the apparatus will cause much pain in the now affected stump of the jaw. On the other hand, the loosening of the remaining teeth will not permit them to be employed as supports for the prosthetic apparatus. Teleky's experience leads him to the conclusion that in spite of all improvements in surgical technique the conservative method of treatment is best.

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**The Mutual Relations of the Sexual Glands.**—SERRALACH AND PARES (*Ann. d. mal. d. org. gén.-urin.*, 1908, i, 881) says that the seminal vesicles are undoubtedly glandular. Having removed the right testicle of a patient, it was observed that on rectal massage of the seminal vesicle of the same side, some of the seminal fluid was seen in the urine. The seminal glands are moreover ejaculatory, because they are surrounded by a layer of muscle. The gland is not a reservoir, as Graf maintained. The finding of spermatazoids in the urine is explained by the fact that by the confluence of the vas deferens and the excretory duct of the seminal vesicle, the self-moving spermatazoids can find their way back into the seminal vesicle as well as pass into the urethra or bladder. The seminal vesicles cannot be the reservoir for the spermatic fluid, because no anatomist has ever found a sphincter capable of forcing the sperm from the vas deferens toward the vesicle, such as the sphincter for forcing the bile to the gall-bladder.

**Antiferment Treatment of Suppurative Processes.**—PEISER (*Zentrbl. f. Chir.*, 1908, xxxv, 777), with Edward Müller, made a report on this subject at this year's German Surgical Congress. Instead of the previously employed small incision with washing out of the abscess cavity, later puncture by a syringe was substituted. After the pus had been evacuated as much as possible, the antiferment, several centimetres less than the pus evacuated, was injected. This was to avoid the production of the pressure of the inflammatory process. The serum, after a few minutes, was withdrawn, and with it usually some pus. Then a new injection was made. Two cases are here reported. In the first there was an increasing, acute inflammatory swelling on the inner side of the right elbow, about the size of the palm of the hand, and pain in the axilla. Some deep fluctuation was detected. About 6 c.c. of thick pus was evacuated by puncture and the serum injected as described. On the following day the swelling had almost completely disappeared. There was no tenderness and no fluctuation. On the fourth day healing had taken place and the patient was discharged. In the second case a similar result was obtained in an abscess of the female breast. A larger number of cases will be reported later. A scar is avoided by this method of treatment.

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**The Treatment of Bony Ankylosis of the Elbow by Means of Transplantation Over the Whole Joint.**—BUCHMANN (*Zentrbl. f. Chir.*, 1908, xxxv, 582) reports two cases in which, after excising the elbow-joint for bony ankylosis following fracture, he transplanted the joint of the first metatarsal joint without opening it, to take the place of the excised elbow-joint. The lower end of the humerus and the upper end of the ulna were suitably notched to receive the bones of the transplanted joint. The metatarsal joint was so placed that its plantar surface was posterior and its dorsal surface anterior, its metatarsal end fitting into the notch in the humerus and its phalangeal end into the notch in the ulna. No bone sutures were employed. The wound in the soft tissues was closed and the elbow dressed in extension and fixed with a plaster cast. The cast was removed twenty-one days later and was replaced by a new one with the elbow in an acute angled position. This cast was removed on the thirty-third day, and on account of a fistula the Bier treatment was applied. The fistula closed after five weeks. In about ten weeks passive movements and massage were begun. Since the removal of the cast active movement within 30 degrees was possible.

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**The Technique of Operation for Cleft Palate.**—HELBING (*Zentrbl. f. Chir.*, 1908, xxxv, 809) has employed the Langenbeck method in 38 cleft palate operations in the past six years. He thinks the bad results are due not to the method, but to the faulty technique. The performance of the operation in two stages, as introduced by J. Wolff, was an important advance. In the first stage the flaps are separated, always with some loss of blood. Four to five days later the sutures are introduced, so that in the meantime the child regains strength. The flap immediately after its separation often suffers for nourishment and is anemic, so that in the interval between the two stages it has time to

recover, and this tends to prevent necrosis. The flaps also thicken, so that they present broader surfaces for approximation, and because of the small escape of blood the sutures can be more accurately placed. In 26 of the 28 cases Helbing obtained a complete closure of the cleft in one operation. The cleft may be so wide and the remaining mucous surface so narrow that the flaps are small, and when brought together they scarcely cover the cleft. The lateral incisions then gape widely and there is much danger that large lateral openings will exist. This danger can be removed by the employment before the operation of suitable apparatus to force the superior maxillæ together. A considerable narrowing of the maxillæ can be obtained in two to three weeks. Many fistulæ remaining after operation can in this way be closed, with the aid of a simple caustic or the thermocautery. No sutures will be necessary. All cleft palates which have been exposed to plastic and mutilating operations on account of the width of the clefts may be closed at one sitting by the Langenbeck operation.

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**Treatment of Burns.**—RENNER (*Zentrbl. f. Chir.*, 1908, xxxv, 907) has obtained very good results during the past year in the treatment of many burns, by the use of a powder consisting of one part bismuth subnitrate and two parts kaolin. With this powder he dressed recent burns without distinction as to their grade of severity. The wound was first cleansed and then dusted with the powder. A layer of sterile gauze was then applied, covered with cotton and fixed with a bandage. The dressing was renewed daily. The chief effect was to dry the wound thoroughly and prevent infection almost completely. In burns of the first and second degrees, after one or two dressings, the wound is covered by a thick firm crust, which favors cicatrization. When the healing is thought to be complete under the crust, the latter can be easily removed by an application of a borolanolin dressing for twenty-four hours. Very rarely a patient will develop an urticarial eruption from the use of the powder. In such cases the powder should be removed by irrigation and only a gauze dressing applied.

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**Aneurysmorrhaphy.**—BINNIE (*Annals of Surgery*, 1908, xlviii, 1) confines his discussion of the subject to a consideration of the possibility of obliterating the aneurysm and at the same time reconstructing the artery in such a fashion that the circulation through it may be restored. He has employed the method as originally outlined by Matas in two cases. The first was reported in 1904. The second was for a popliteal aneurysm developed in a man, aged sixty-seven years, with a history of severe trauma in the same leg three years before and a second severe strain of the foot three weeks before the operation. The tumor on being opened was found filled with soft, black, non-lamellated blood clot. The cavity had no distinct walls, and was the size of two large fists. Removal of the clot exposed a ruptured aneurysm as large as a medium-sized orange communicating with the larger cavity. The walls of the aneurysm were fairly healthy. On splitting the true aneurysm two arterial openings were found, one to one and one-half inches apart. Fairly healthy arterial wall consisting of two-thirds of the circumference



united the two openings and formed a groove on the bottom of the sac. The artery was reconstructed around a No. 15 Fr. catheter, thus closing the communication between the artery and sac. The sac was obliterated by continuous catgut suture. The aneurysm was cured, but it could not be proved that the circulation was reestablished through the vessel. In another case a similar operation was performed, but the sac was too imperfect to permit of its obliteration. Ligation of the femoral artery was necessary later for hemorrhage and finally amputation. Section through the artery showed the interior slightly irregular, with a definitely thickened wall, surrounded by a mass of inflammatory tissue. The closure in the artery persisted for two weeks, and then only about a third of the line of union gave way. The arterial wall was markedly degenerated, the line of suture was absolutely unsupported by surrounding structures and lay exposed in the cavity of a false aneurysm.

ABBE (*Annals of Surgery*, 1908, xlviii, 10), for an aneurysm of the gluteal artery, first placed a temporary ligature on the external iliac artery, and then incised the gluteus muscle to the aneurysm. By pressure it could be emptied, and when the pressure was removed it quickly filled up again. The sac was opened and the opening of the gluteal artery was plugged by the index finger. With a continuous suture of the internal wall of chromicized catgut the arterial opening was closed and then the entire sac was obliterated. Recovery was immediate. This shows that reliance may be placed on the plastic union of the opposing walls of an artery.

BLAKE (*Annals of Surgery*, 1908, xlviii, 15) reports a case of popliteal sacciform aneurysm in which the artery was on the superficial side of the sac. The communicating opening between the artery and the sac, about 1 inch long, was less than one-half inch from the incision in the sac. The Matas restorative operation was, therefore, impossible. The communication, however, was fairly effectively closed with a single row of chromicized catgut sutures which also considerably narrowed the lumen of the artery. It being impossible to make the suture line more secure, the artery was ligated on the proximal side of the aneurysm. The sac was obliterated and the wound closed without drainage. Three months later there was no sign of a recurrence. Blake thinks that the obliterative operation is best for popliteal aneurysms, and points to the fact that the only relapses reported from the Matas operation have followed the reconstructive operations on popliteal aneurysms.

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**The Treatment of the Appendix Stump after Appendectomy.**—WILLIS (*Annals of Surgery*, 1908, xlviii, 74) received communications from 105 representative surgeons concerning their methods of treating the stump in appendectomy. The chief interest lay in the answers to the question as to whether the stump was buried, and why it was or was not. Of the 105, 77 surgeons always bury the stump, 66 by ligating and inverting into wall of the cecum, 11 by invaginating the ligated stump in the cecum; 11 usually bury the stump (leave unburied only in drainage cases); 3 have no settled method; 2 leave no stump; 11 never bury the stump; 1 does not answer the question; 23 make mention of untoward results that have followed simple ligation and leaving the stump unburied.

These consisted of intestinal obstruction from adhesions; fecal fistulæ; peritonitis; persistent suppuration; slipped ligatures; abscess from leakage of stump; and adhesion of Fallopian tube to appendix stump. Only 2 out of the 105 surgeons reported that they have ever observed harmful effects of any character after burying the stump. In one a stitch abscess gave way during the first defecation (after calomel), and a large exudate developed with the symptoms of perforation. The exudate was absorbed and the patient recovered. In 2 other cases there were secondary abscesses. Although no inquiry was made as to the incidence of hemorrhage, 10 out of the 105 replies contained statements in regard to this point, and in several cases the abdomen had to be opened because the patient was almost pulseless. Postoperative pain as an argument for the unburied stump is not supported. The chief objections to leaving the stump unburied are: (1) Obstruction to the bowel; (2) slipped ligature, with escape of fecal contents into the abdominal cavity; and (3) adhesions to the raw surface of the stump. Distension of the bowel may occur after any abdominal operation. It is easy to understand how the increased pressure within the bowel may balloon out the appendix stump into a pyramidal-shaped body, with the apex at the ligature. The integrity of the bowel wall is thus jeopardized in every case in which any distension occurs.

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**A New Method of Performing Prostatectomy.**—WILMS (*Deut. Ztschr. f. Chir.*, 1908, xciii, 325) obviates the excessive injury to the bladder of a transvesical operation and the danger to the rectum of a perineal operation, by attacking the prostate and enucleating it through a lateral incision in the perineum. The prostate even when not markedly enlarged, projects into the perineum under the pubic arch, so that even by a lateral incision it is easily accessible. He makes the incision about 4 to 5 cm. long along the left pubic ramus. After the division of the thin fascia one finds a loose connective tissue, traversed by a few veins, which separates easily without bleeding, so that the lateral lobe is readily exposed. In thin people the wound will be scarcely 1.5 cm. deep. The ischiocavernosus muscle, and with it the internal pudic artery and its branches, can be pushed toward the median line without exposing these vessels. A catheter is introduced into the urethra, the capsule over the left lobe of the prostate is opened, and the enucleation is carried out with the finger. A slight resistance is met with on the anterior surface of the prostate. The prostatic portion of the urethra is removed, as in the operation through the bladder. Wilms performed this operation in 3 cases. An injury to the rectum is impossible, since one works within the capsule. His results have convinced him of the superiority of this over other operations.

## THERAPEUTICS.

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**Alcohol Injections in Blepharospasm.**—VALUDE (*Tribune méd.*, 1908, xli, 232) considers that injections of 80 per cent. alcohol combined with cocaine or stovaine are a safe, simple, and effective means of treatment of obstinate facial spasm. The treatment is applicable both in simple spasm and in the complicated facial tic douloureux. The injections should be made at the point of emergence of the facial nerve. The paralysis which follows the injections should cause no anxiety, no matter how long it lasts, so long as there is no tendency to alteration of the cornea and the eyes close sufficiently during sleep, and if there is no ptosis of the lower eyelid; such paralysis needs no treatment unless the integrity of the cornea is threatened.

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**Morphine in Laryngeal Diphtheria.**—LESAGE and CLERET (*Tribune méd.*, 1908, xli, 213) believe that in the asphyxia of diphtheretic croup the hypodermatic administration of morphine will often obviate the employment of intubation and, even when this operation is essential, that morphine will greatly lessen the length of time that the tube is left in the trachea. Generally the tube may be withdrawn in twelve hours. Of course the morphine is used in connection with antitoxin. Lesage and Cléret find that morphine is not dangerous to and is well borne by young infants and that by its employment intubation in many instances may be avoided even when it seems necessary. The use of the drug consequently obviates the occurrence of the laryngeal lesions which may be caused by the presence of the tube and the sleep which it induces increases the patient's power of resistance to the infection. The dosage is regulated in accordance with the age of the patient.

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**Action of Sodium Bicarbonate on the Gastric Secretion.**—HAYEM (*Tribune méd.*, 1908, xli, 281) considers that the alkalies are absolutely contra-indicated in hypo-acidity while in hyperacidity they have two indications. They may be employed in the tardy pain of hyperacidity, but the tendency of the patient toward abuse of the medication must not be forgotten for excessive use may cause a gastritis medicamentosa. Hayem, is, even here, inclined to prefer bismuth subnitrate in large doses to the alkalies. In hyperpepsia the alkalies may be employed to modify the digestive process; here the so-called Vichy cure may prove beneficial. The employment of artificial Carlsbad salt seems, however, in Hayem's opinion, to be of greater advantage.

**The Vaccine Treatment of Gonorrhoeal Vulvovaginitis in Children.**—BUTLER and LONG (*Illinois Med. Jour.*, 1908, xiii, 538) have employed the treatment by means of bacterial vaccines in a number of children afflicted with vulvovaginitis and conclude that this form of therapy has a distinct place in the treatment of gonorrhoea in the female and that it appears to be far more efficient, at the same time scientifically more tenable, than local antiseptic treatment. The vaccinations were employed on the basis of the opsonic index and Wright's technique was adhered to. The vaccinations were interspaced according to the index, an effort being made to inject the patient before the index declined below normal. Butler and Long do not feel justified in generalizing as to dosage nor in making any statement as to the time that the index will remain above normal after vaccination. The dosage varies in different patients and can be determined only by investigating for each individual the immunizing response to a given dose as indicated by the index.

**Results in Bacterial Vaccine Therapy.**—HOLLISTER (*Ill. Med. Jour.*, 1908, xiii, 28) sums up his conclusions as to the value of vaccine therapy thus: (1) Inoculation by autogenous vaccines, properly administered and regulated, is one of the best—if not the best—method of curing and preventing the recurrence of chronic staphylococcic infections, such as furuncles, etc. (2) In chronic acne injections of autogenous vaccine of staphylococcus often cures and usually causes marked improvement. (3) In localized tuberculosis—osteitis, arthritis, adenitis, etc.—the administration of tuberculin, as guided by the opsonic index, is frequently of distinct value, acting both as a general tonic and hastening local repair. (4) Judging from the literature and from personal experience, it may be said that occasional marked results may be expected in chronic local infections by the colon bacillus (cystitis, pyelitis, etc.) and by the gonococcus (arthritis).

**Suprarenal Extract in Cardiac Collapse.**—KOTHE (*Zentralbl. f. Chir.*, 1907, xxxiii, 969), in two patients, who had been subjected to spinal anesthesia followed by complete collapse, and in whom ordinary measures had proved of no avail, succeeded in restoring the function of the heart in ten seconds by means of injections of a solution of suprarenal extract. He concludes that the intravenous injection of 0.05 milligram of this substance should be capable of saving life in certain instances; at any rate, further trial of the procedure is advisable.

**Combined Treatment in Malignant Tumors.**—BACK (*Berl. klin. Woch.*, 1907, xlv, 1335) strongly advocates the use of the knife combined with the employment of the Röntgen rays in malignant growths. His usual technique consists in as thorough extirpation as possible; after about a week the rays are applied every two days, for a sufficient time to produce a reaction. If the growth is extensive, it is better not to close the wound until the rays have been employed for about a week; at the end of this time the wound may be sutured and after another week the use of the rays should be begun again. At first a diaphragm is used; later is not employed. The author uses the knife at the beginning of treatment even in the small epitheliomas which the rays alone will cure.

In order to insure the proper effect from the rays it is necessary to obtain the characteristic local reaction.

**Large Doses of Antitoxin in Diphtheria.**—DELEARDE and MINET (*Province médicale*, 1907, xx, 501) emphasize the importance of large doses of antitoxin, even in mild types of diphtheria, on account of the possibility of the occurrence of serious complications and sequels. Their observations prove the harmlessness of large doses, their influence in the management of toxic symptoms, their rapid curative action, and their effect in preventing complications. Their usual initial dose is about 50 c.c., and this amount has never been followed by any serious accident. Further dosage is regulated by the patient's progress, but there need be no hesitation in giving 100 c.c. within twenty-four to thirty-six hours. By the third day the temperature usually reaches normal, the membrane becomes detached and is expectorated, and recovery is rapid. The albuminuria, which is a positive indication for the administration of large doses, quickly disappears, and eruptions due to the injections are rarely seen. Supplementary treatment, consisting of applications to the throat of camphor, 2 parts; menthol, 1 part; lavage of the mouth with 5 per cent. Labarraque's solution; warm baths every morning; and, in the presence of bronchitis, two sinapisms to the chest daily, is advised. Mild expectorants may hasten the elimination of the exudates. Intubation should be done if necessary, and to these patients inhalations of steam impregnated with tar or eucalyptol are given. The proper diet is one which is poor in chloride elements and frequent drinks should be administered. Antipyretic drugs are contraindicated.

**The Treatment of Tuberculous Adenitis.**—ROBIN (*Tribune méd.*, 1908, xli, 249) advises, in addition to climatic and general tonic treatment, the evacuation by puncture of suppurative adenitis and the injection of a mixture of iodoform, 1 part; ether, 10 parts; oil of sweet almonds, 100 parts; creosote, 2 parts. In chronic cases of the affection cure may be effected in two or three months after a score or so of punctures.

**Bleeding in Pneumonia.**—WEST (*Practitioner*, 1908, lxxx, 429) considers that when the lungs are greatly engorged, the patient cyanosed, and the right heart overdistended, great relief may be given by bleeding, but the bleeding must be free and rapid. Several ounces—a pint or a pint and a half—should be withdrawn rapidly from a large vein. As the blood flows, the color improves, the heart action becomes less labored, and the urgent symptoms may disappear. The loss of so much blood leaves the patient weak, and such a bleeding is, therefore, suitable only in special instances. The typical patient is a young, full-blooded, healthy, well-fed adult, with florid complexion and well-developed muscles. Bleeding is contra-indicated in the weakly, thin, and anemic, in the young, and in the aged. In selected patients free bleeding is of great use, and doubtless has saved many lives, but prejudice is likely to prevent its employment in private practice. Venesection is sometimes spoken of as useful on theoretical grounds, because, with the blood, some of the toxins of the disease are also removed, but the author thinks this theory a mischievous one, since it may lead to

bleeding in unsuitable instances. Hypodermatoclysis of normal saline solution has been advocated as a way of diluting the toxins or assisting their elimination, but it is not favorably regarded by West, as it does not seem to him to be founded on sound theory.

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**The Comparative Therapeutic Value of Iron Compounds.**—VAN GIESON (*New York Med. Jour.*, 1908, lxxxvii, 687) sums up a study of this subject with the following statements: A careful study of iron metabolism shows that the official preparations of iron so long useful in the past will increase hemoglobin. The ferrous carbonate, the soluble oxide with sugar, the double salts with the vegetable acids, the solution of the perchloride given in combination and largely diluted with milk, are the forms most likely to produce good results. Directly conflicting views as to the value of modern proprietary preparations exist among competent observers. In all iron medication the question of defective metabolism is important. Patients must be individualized, and preparatory treatment is essential. Rest in bed, massage, milk diet, unfermented grape juice, and static electricity are valuable adjuvants preparatory to ordering the administration of iron compounds.

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**Cholesterin in Therapeutics.**—ISCOVESCO (*Tribune médicale*, 1908, xli, 154) has proved that cholesterin protects the human red blood cells against serums and other hemolytic substances. In consequence, he has administered this substance in a number of patients affected with rheumatic purpura, chlorosis, pulmonary tuberculosis, infantile lymphatism, etc. In every patient observed he has obtained a cure or a distinct improvement. In pulmonary tuberculosis the treatment brings about a rapid amelioration of the general condition without a parallel improvement in the pulmonary lesion. Cholesterin must be administered in emulsion.

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**Opium.**—CROUZEL (*Journal de médecine de Bordeaux*, 1908, xxxviii, 69) considers that the different effects produced by opium are due, in considerable measure, to the fact that all opiums do not contain like amounts of the principles of this drug. He quotes Smith to the effect that a good opium should contain principles in the following proportions: Morphine, 10 per cent.; narceine, 0.02 per cent.; codeine, 0.3 per cent.; papaverine, 1.0 per cent.; thebaine, 0.15 per cent.; narcotine, 6.0 per cent.; meconine, 0.01 per cent.; meconic acid, 4.0 per cent.; lactic acid, 1.25 per cent. He believes that until we are able to obtain a standardized opium any certain and constant action of the drug to get such a standardization, while difficult, should not be impossible, and advises that a special service to oversee the manufacture of opium should be organized.

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**Lactic Acid in Nasal Conditions.**—MACCOY (*Monthly Cyclopedia of Practical Medicine*, 1908, xxii, 51) considers that the employment of lactic acid in nasal obstructions due to engorgement or hypertrophy offers advantages over other acids in that it is less severe in action and reaction, while it is none the less efficient. It is superior to other acids by reason of its power to change cell acids and quicken changes in the mucous membranes, effecting absorption of cell tissue in a remarkable

manner. It does not produce cellular irritation in contiguous tissue when locally applied, and is therefore of greater value than any other chemical agent now employed, and, while it has a cauterant action on mucous tissue, it also has a special selection for cell tissue, making its effects apparent by absorption of hyperplasia.

**The Excretion of Hexamethylenamine (Urotropine) in the Bile and Pancreatic Juice.**—CROWE (*Johns Hopkins Hospital Bull.*, 1908, xix, 109) has performed certain experiments with this drug with the intent to ascertain its value in infections of the gall-bladder. He believes that before its value can be definitely established further work must be undertaken. He summarizes his results as follows: (1) After its administration by mouth, hexamethylenamine appears in the bile and pancreatic juice of dogs. It finds its way into the bile through the liver and through the wall of the gall-bladder. (2) It has been demonstrated in the bile, cerebrospinal fluid, saliva, pleural effusion, and blood of man. (3) When given in sufficiently large doses (75 grains per day), it appears in the bile in quantities which suffice to exercise a decided bactericidal action.

**The Treatment of Tapeworm.**—SCHILLING (*Therapeutische Monatshefte*, 1908, xxii, 187) gives in the morning, fifteen minutes after a breakfast of coffee with zwieback, the following formula, which has acted well in his hands: Fresh ethereal extract of male fern, 2 to 2½ drams; powdered jalap, 7½ grains; simple syrup, sufficient to make 1 ounce. This mixture should be well shaken. The parasite usually appears in three to four hours. Schilling considers it unnecessary that the teniafuge should be taken fasting, but if evacuation of the bowels does not take place or is delayed, he advises the employment of an enema of about a quart of warm water.

## PEDIATRICS

UNDER THE CHARGE OF

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**Hygiene of the Eye in School Children.**—Concerning this subject W. M. CARHARDT (*Amer. Jour. Obstet.*, July, 1908) summarizes his article as follows: (1) The increase of late in the number of children wearing glasses is not due to an increase in the number of weak or diseased eyes so much as it is due to the greater strain upon the function of vision necessitated by our more extended use of the eyes for close work in the complex civilization of the present day. (2) The normal child is born hypermetropic and without astigmatism. The myopic child is either defective from birth or has acquired myopia from the stress of eyestrain, usually through the "turnstile of astigmatism." Astigmatism is not congenital, but is practically always acquired in the normal child

during the early years of life by excessive strain upon the muscles of accommodation. (3) Kindergarten and primary work should be arranged so as to avoid strain upon the muscles of accommodation of the eye in the plastic years of childhood. Hence, sewing and all weaving exercises should be limited in amount, if not absolutely eliminated. (4) Systematic study should be only begun when the delicate and soft tissues of the child's eyes have attained sufficient formation to resist distortion on moderate use of the accommodation. This means that prolonged close work should not be allowed until the age of ten years or over. The child beginning systematic work at that age will, with suitable care, be able at sixteen or eighteen years to acquire all the knowledge possible to its more precocious companion, and will have the inestimable advantages of normal eyes and healthy physique. (5) No young child should be encouraged to compete with its companion for prizes. Mental and ocular overstrain are the inevitable results of such educational monstrosities. In the primary schools, especially, there should be no grading of the children. (6) A child incapable of the prolonged use of the eyes at the proper age should not be classed as culpably lazy. In the majority of cases there will be found uncorrected refractive errors. (7) Inability to concentrate the mental attention, and deficient powers of observation are often caused by bad visual memory resulting from eyestrain. (8) The symptoms and physical signs of eyestrain in children can be easily recognized, and there is no more brilliant success in medicine than follows a correction in children of refractive error. Ocular hygiene is all important in preventing educational overstrain.

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**Röntgen Diagnosis of Infantile Scurvy.**—KLOTZ (*Monats. f. Kinderheilk.*, 1908, vii, 36) reports such a case in a child aged nine months, in which the only signs present were a slight swelling of the distal end of the left femur, and marked pain whenever picked up or even touched; there was no gingivitis, no bleeding from the gums, no hematuria, no petichiae, no anemia. The Röntgen pictures, however, were very typical of the disease; a marked thinning of the cortex, a disappearance of the sharp outline of the bone, loss of the structural outlines near the epiphyses, separation of the periosteum, bending of the bones, etc. He says that all suspicious cases of this disease should be examined with the Röntgen apparatus.

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**Paratyphoid Fever and Melena in the Newborn.**—C. NAUMERCK and E. FLINZER (*Münch. med. Woch.*, 1908, i, 1217) performed an autopsy on a child thirty-six hours old whose death was said to have been due to melena. The autopsy revealed multiple necroses of the gastric mucosa, otitis media, cholecystitis, slight enlargement of the spleen, and hemorrhagic diathesis. The stomach and intestines were filled with clotted blood and some mucus. The bacteriological blood examination revealed an organism which could be identified with paratyphoid bacillus (Schottmüller); diagnosis was made from cultures, agglutination tests, and animal experiments. Further investigation showed that the infection was of intra-uterine origin, the mother having suffered four weeks before the birth of the child from violent diarrhoea, which lasted eight days; there was also headache, nausea, vomiting, abdominal pain, and



fever; the condition improved after a time without treatment. The woman had probably been infected by eatables, which had been sent her from her home, a place which about that time had many typhoid and typhoid-simulating cases. The blood of the mother agglutinated the bacillus from the child in dilutions of 1 to 400. Whether the infection arose through the amniotic fluid being contaminated with the paratyphoid bacillus, or whether as a primary blood infection through the placental circulation, the authors could not decide.

**The Behavior of the Cutaneous Tuberculin Reaction during Measles.**—C. VON PIRQUET (*Deut. med. Woch.*, 1908, xxxiv, 1297) has found from the study of a large number of patients with measles, some of which were known to have tuberculosis, that tuberculous children lose their reaction to tuberculin during the measles attack for about a week. One hundred and fifty-nine patients with measles were examined: 50 only during the week following the beginning of the eruption, and all of these were always negative; 36 negative both during and after the week of eruption; 2 negative before, during, and after the week of the eruption; 6 negative before and after the eruption week; 23 negative, examined only after the eruption week; 3 positive, examined only after the eruption week; 25 examined during and after eruption week, first negative and then positive; 6 examined before, during and after, with respectively positive, negative, and positive results; 1 before and during the eruption week, first positive and then negative; 1 during and after the eruption week, first negative and then positive; and 6 with uncertain reactions. This phenomenon von Pirquet believes to be due to a destruction of the tuberculosis antibodies; in corroboration of this he has found that during measles the tuberculous process has spread considerably in every case in which the condition has been known to exist. The disappearance of the reaction does not occur in scarlet fever, diphtheria, epidemic cerebrospinal meningitis, or typhoid fever. In cases in which the tuberculin reaction persists or exists during an eruption resembling measles, von Pirquet is certain that the exanthem is other than measles, thus giving the existence of the tuberculin reaction a value from the standpoint of differential diagnosis.

**Rickets and Scoliosis.**—E. KIRSCH (*Deut. med. Woch.*, 1908, xxiv, 1309) has made a series of observations to determine how many cases of scoliosis rest upon a rachitic basis, and in how many the condition is progressive; and whether all fixated scolioses are of rachitic origin and whether a scoliosis originating during school life can become fixated. The distinction between fixated and non-fixated scoliosis is thoroughly considered. In all 1015 children (518 boys and 497 girls) were examined; 493 children (217 boys and 276 girls) belonged to the lower classes, and 522 (281 boys and 241 girls) to the upper classes. The scolioses at the beginning of school life amounted to 20.5 per cent., in the upper classes to 30.4 per cent., but it is only the habit scoliosis which thus increases. In girls the increase is from 14.4 to 28.2 per cent.; in boys from 11.8 to 15.4 per cent. The fixated scolioses, on the other hand, increase only from 7.3 to 9.4 per cent.; among boys the number actually decreases from 7.2 to 6 per cent.; among girls it increases from 7.4 to 12.9 per cent. He formulates the following

conclusions: (1) A large number of habit scolioses develop during school life, but only a few fixated cases, and they are only slightly fixed; more cases occur in boys than in girls. (2) Seven times as many cases of fixated scoliosis exist at the beginning of school life than develop during these years; during school years the fixated cases deteriorate more in boys than in girls. (3) Most all fixated cases, when not congenital, are of rachitic origin. (4) The oblique position of a school child, which does not produce any fixation symptoms, leads to a light type of scoliosis; after some years it may show a few clinical fixation symptoms. (5) The explanation for this is found in the fact that habit scoliosis and fixated scoliosis are two separate diseases; pathologically the former is a primary joint contraction, the latter a bone deformity; etiologically the latter depends upon rickets, the former not; clinically the former is a non-fixated lateral curvature, the latter is associated with torsion and fixated curvature; prognostically the former is capable of spontaneous improvement, the latter is not; therapeutically the former is easily influenced in every stage, the latter only if treatment is begun before the child is sent to school.

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**Tuberculosis of Nursing Infants.**—A series of postmortem examinations performed by ENGEL (*Monats. f. Kinderheilk.*, 1908, vii, 28) has prompted the following conclusions: In well-nourished infants, and more particularly in breast-fed infants, tuberculosis is almost invariably localized to the glands, and if found in the lungs, the foci are usually small and surrounded by a thick, tendinous capsule; if death resulted in these cases it was invariably due to an acute bacillary invasion, which induced the fatal termination by setting up an acute miliary tuberculosis. In poorly fed, emaciated children, however, the appearance even before beginning treatment led to a suspicion of graver organic disease; examination invariably revealed chronic tuberculosis of one or more organs, chronic confluent miliary tuberculosis, caseous peribronchitis, etc. The emaciation noted in such children is not due to the disease, but has rather preceded it, and is therefore entirely independent of the organic disturbance. It is probably true that because of the miserable nutritional state the organs become involved, while in well-nourished children the disease remains localized to the glands. Of breast-fed children dying of tuberculosis in his service, only 8 per cent. died of caseous pneumonia, while of the other children, this disease was found in 70 per cent. of the cases studied after death. Engel further believes that breast milk protects the infant to some extent from tuberculosis.

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**The Exudative Diathesis.**—CZERNY (*Monats. f. Kinderheilk.*, 1908, vii, 1) finds that in all instances in which children suffer with the exudative diathesis, parents and other relatives are neuropathic or psychopathic; in fact, he says, children of markedly nervous parents are rarely free from this constitutional affection, but there is not necessarily a relation between the degree of nervousness in the parent and the exudative diathesis in the children. Knowledge of this combination is of marked practical importance, as a complete cure can be expected only if the treatment is directed both against the diathesis and the neuropathic tendency. A persistent eczema may be cured by simply removing the child from its family surroundings and placing it where its mental

activity can be guided along different grooves; the same is true of many cases of nervous asthma and other nervous affections. Czerny advises against rest cures and medicines, preferring an entire change of the method of living and education.

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## OBSTETRICS.

UNDER THE CHARGE OF

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**Delivery by Forceps in Contracted Pelvis.**—CHAMPNEYS (*Jour. Obstet. and Gynec., Brit. Emp.*, June, 1908) reports the case of a patient having a contracted, flat, reniform pelvis, with slight scoliosis, the true conjugate being  $2\frac{1}{2}$  inches, who was delivered by the induction of labor, at the thirty-second week, by the aid of forceps. The child, sixteen and one-half years afterward, is living and in good condition. Labor was induced by the use of bougies and laminaria tents. One week's time was occupied in inducing labor pains. The head did not engage as there was almost entire uterine inertia. The head was pressed down on the brim where it occupied a transverse position. The forceps was then applied, using the right blade somewhat behind the occiput, and the left blade in front of the sinciput, the blades were locked and the head extracted without much difficulty. When the head emerged the blades were at the sides, as rotation in the forceps had occurred. Attention is called to the fact that in transverse application of the forceps, the application should also be oblique. In order to favor anterior turning of the occiput the occipital blade should be placed behind the occiput and the other blade in front of the other extremity of the head. With these precautions anterior rotation is more apt to occur. Champneys concludes that while he was thus successful in 1891 in delivering the patient with forceps, that in 1908 he would certainly have performed Cesarean section.

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**Collargol in the Treatment of Puerperal Infection.**—BONNAIRE and JEANNIN (*L'Obstétrique*, April, 1908) report 49 cases of puerperal infection treated by the intravenous infection of collargol. They divide their cases into one group of three, in which the injection was made as a prophylactic measure. These were cases infected at the time of labor, and the treatment was carried out without waiting for the development of fever after delivery. In 3 cases the result is stated as "unknown," as the patients passed from under observation before a definite conclusion could be drawn. In 10 cases death occurred. In 15 cases it is thought that the patient's cure did not depend upon the use of collargol. In 4 cases the use of collargol is said to have been "not decisive." In 14 cases its use was followed by prompt and immediate improvement. The treatment was carried out, as a rule, before the eleventh day after

labor; in one case as late as the thirty-first day after the development of infection. The highest number of injections was four, the lowest number one. Following these injections many of the patients had a chill more or less violent. Variations were observed in the condition of the blood, and increase in leukocytes usually was present. The effect of the remedies seemed to be transient; in most cases the patient soon returned to her original condition. The disadvantages of the method are injuries to the vein, the possible development of embolism, and the disturbance which followed the injection as demonstrated by the chill. The quantity employed varied from 2 to 4 c.c. The actual dose was computed to be less than 10 c.c. A solution of 1 to 100 was used. Of this solution from 10 to 15 c.c. was the usual injection. We believe that these results are vitiated and unreliable by the fact that other methods of treatment were employed in these cases. These patients were curetted and received frequent intra-uterine irrigation. In our experience these procedures, especially repeated intra-uterine douches, serve to maintain a condition of infection which would render the use of another remedy misleading and ineffective. To demonstrate clearly the value of the method employed, no interference with the uterus should have been practised and no other treatment instituted except the free use of food, and the proper regulation of the intestinal action.

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**Chorea during Pregnancy.**—SHAW (*Jour. Obstet. and Gynec., Brit. Emp.*, June, 1908) reports 3 cases of chorea complicating pregnancy, which he treated upon the supposition that toxemia was the essential cause of the chorea. These patients were put in bed and given eliminative treatment in the most efficient manner possible. In 1 case, which did not yield rapidly to calomel and salines, a diuretic mixture and 5 grains of thyroid extract three times daily were also employed. This treatment proved eminently successful, the patient sleeping without sedatives. Shaw does not believe that the interruption of pregnancy is indicated in these cases. The success of the treatment employed is a striking evidence of the correctness of his conclusions.

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**The Suprarenal Capsules in Eclampsia and Nephritis.**—CHIRIE (*L'Obstétrique*, April, 1908) has examined the suprarenal capsules in cases of toxemia and has reviewed the literature of the subject. He concludes that in eclampsia, retroplacental hemorrhage, and in the nephritis of pregnancy cortical hyperplasia is present in the suprarenal capsules; less frequently the hyperplasia is medullary. The cortical changes very probably depend upon the undue toxic tension of the gland, and are less influenced by its angiotoxic tension. The medullary hyperplasia seems to depend largely upon the cardiac hypertrophy usually seen in these cases. The angiotoxic tension of the medullary substance is recognized and acknowledged, although its exact relation to the changes seen in nephritis has not been made out. In all of the cases studied the suprarenal hyperplasia was secondary to the lesions observed in the kidneys.

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**Typhoid Fever Complicating Pregnancy.**—FRENCH (*Brit. Med. Jour.*, May 16, 1908) believes that there is no special time in typhoid fever when a pregnant patient is especially likely to abort. Some women

pass through typhoid fever without interruption of pregnancy, and give birth to healthy children. Labor is attended with very little apparent suffering, and the patient seems usually much relieved by the expulsion of the child. Involution seems to go on fairly well, and the course of the typhoid fever is not much influenced by the labor. The mortality of typhoid fever complicated by pregnancy is stated by French as 14 per cent.; others give a mortality of from 16 to 17 per cent. In 65 per cent. of French's cases pregnancy was interrupted; while others give a lesser frequency in the interruption of gestation. It has been clearly demonstrated that the active agents of typhoid infection may pass from the mother to the foetus. Again it is probable that the foetus in its turn can infect the mother. Where foetal infection does occur and pregnancy is interrupted the child has been found with some of the characteristic lesions of typhoid fever. The absence of intestinal ulceration in the foetus is no proof that the child has not had infection in the uterus. It is impossible in our present knowledge to state whether a foetus which survives typhoid fever and goes to term would be immune afterward. As regards the interruption of gestation by the obstetrician, it is thought, when viability is present and there is great desire for the life of the child, that pregnancy may be interrupted. This is done because the danger of foetal infection increases with each day of the fever.

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**The Lower Uterine Segment.**—BARBOUR (*Jour. Obstet. and Gynec., Brit. Emp.*, May, 1908) concludes an illustrated paper on this subject as follows: Several cases have been reported in which the decidual reaction extended below the internal os. These are best described as aberrant types. Proof has been given that in the section described by Barbour the decidua extended below the retraction ring. The shorter the cervix the greater is its thickness. In Barbour's section the retraction ring is some distance above the internal os. This is not a distended cervix, but part of the wall of the uterine body. In rupture of the uterus the tear is incomplete so long as it is lateral, but when it extends to that part of the uterus which is covered by peritoneum it becomes complete.

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**Intra-uterine Death of the Foetus in Six Consecutive Pregnancies.**—This interesting case is reported by WILLIAMSON and HOLLAND (*Jour. Obstet. and Gynec., Brit. Emp.*, May, 1908) with illustrations. The patient gave no physical signs of syphilis nor could any history of possible infection be obtained, nor was there found any abnormal condition in the pelvis to account for the death of the embryo. Neither she nor her husband had followed any occupation likely to bring about such a result. She was delivered of a still-born macerated child in the hospital, supposed to be about thirty-six weeks' gestation, the centre of ossification in the lower portion of the femur not having appeared. A very thorough microscopic study of the foetus was made and resulted in finding *Spirocheta pallida* distributed throughout the liver and spleen. The arrangement of the spirocheta around the bloodvessels of the embryo did not justify the assumption that the infection began in the placenta and reached the foetus through the vessels. In view of the results of the examination of the foetus the parents were again very closely questioned and both were thoroughly examined. Nothing could be found pointing

clearly to syphilitic infection. The patient became pregnant again without menstruating and was treated by mercury and iodide of potassium. Labor was induced and twin children were born, evidently premature. One of the amniotic sacs contained a large excess of fluid. Labor had evidently been induced too soon, the twin pregnancy and polyhydramnios causing abnormal size of the uterus. The children died after a few days and were thoroughly examined and no *Spirocheta pallida* were found.

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**Transverse High Position of the Head and Face Presentation and its Treatment with Forceps.**—ZIEGENSPECK (*Zentralbl. f. Gynäk.*, 1908, No. 24) calls attention to the possibility of delivery of these cases by the use of forceps. He states that the simplest instruments should be employed, and not those with elaborate mechanism. The operator must vary the line of traction as the head comes down, and especially endeavor to protect the perineum. The instruments are applied to the sides of the head and rotate with the head. Ziegenspeck has had several cases in which the chin was brought to the front and labor completed successfully.

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**Cesarean Section for Stenosis of the Vagina.**—DAS (*Jour. Obstet. and Gynec., Brit. Emp.*, May, 1908) reports 3 cases in which patients were delivered by Cesarean operation because the lower birth canal was so contracted as to make delivery impossible. One of the cases had been operated upon for vesicovaginal fistula without success. There was great contraction of tissue and the vagina was very much narrowed. The patient failed to report at the hospital until she had been for some time in labor. She was then delivered by section, but died after the operation, with abdominal distention. The child survived. The second case had contracted pelvis and had been delivered by forceps of a dead child, followed by septic infection and cicatricial contraction of the vagina. The foetus was transverse and no heart sounds could be heard. The patient was delivered by celiohysterectomy, making a good recovery. The child was dead at the time of operation. The third patient had had a very difficult labor, followed by sloughing of the whole base of the bladder; there was also a rectovaginal fistula. This was considerably improved by operation and the patient became pregnant. She was delivered by celiohysterectomy, and the stump, although not on the abdominal surface, was kept outside the peritoneal cavity to avoid the danger of infection from the fistula. Mother and child made good recoveries.

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**Amniotic Liquid as a Possible Cause for Eclampsia.**—ALBECK and LOHSE (*Ztschr. f. Geb. u. Gyn.*, 1908, Band lxii, Heft 1) conducted experiments with the amniotic liquid of patients having eclampsia. To determine its toxic properties and its influence in producing eclampsia, the amniotic liquid was taken from typical cases in which there had been abundant convulsions. It was injected into pregnant animals and multiple necrosis was found in the liver of the animals, corresponding microscopically to the lesions found in the human subjects dying of eclampsia. Injections proved in some instances fatal to the animals, while in others the animal was depressed for a short time and then recovered.

## GYNECOLOGY

UNDER THE CHARGE OF

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**Prolapse of the Female Urethra.**—G. F. BARBOUR SIMPSON (*Surg., Gyn., and Obstet.*, 1908, vi, 512) reports a case of prolapse of the female urethra in which the redundant tissue was angiomatous. Resection was done. Simpson says the treatment should first of all be directed to the relief of any causal condition, as cystitis or calculus. One may try to relieve the inflammation of the protruding mucous membrane by the local application of hot water and rest in bed, when simple reduction by manipulation or aid of a sound may be attempted, followed by the use of astringent injections, with a view to promoting contraction of the urethral canal. This may succeed in cases in which there is but slight eversion present, but, as a rule, some form of operative interference will be required as in the case described.

**Immediate vs. Deferred Operation for Intra-abdominal Hemorrhage Due to Tubal Pregnancy.**—The first feature of the scientific work of the American Gynecological Society in May, 1908, was a symposium on this subject (*Amer. Jour. Obst.*, 1908, lviii, 8) and the papers furnished by Janvrin, Montgomery, Frederick, Manton, Laphorn Smith, Baldy, Krug, and others, and the discussion following furnished a good exposé of the subject. The preponderating evidence offered was that every case diagnosed as ectopic pregnancy should be operated on at some time. If early, and particularly if rupture has occurred, the operation should be done at the earliest practical moment, if the shock incident to rupture and hemorrhage were apparently not too great to permit recovery from operation. In late cases in which viability was probable careful watching with operation shortly before full term or operation at once should be done. In the very hazardous, early cases excessive shock and hemorrhage should not preclude hasty securing of bleeding vessels by laparotomy and the application of suitable measures to reduce shock and the bad effects of excessive blood loss. The abdominal instead of the vaginal route was strongly advocated.

**Primary Ovarian Pregnancy.**—C. C. NORRIS and C. B. MITCHELL (*Surg., Gyn., and Obstet.*, 1908, vi, 460) report a case of primary ovarian pregnancy operated upon by J. G. Clark. Norris and Mitchell claim to have found 16 positive cases, 15 probable, and 9 fairly probable. From this list is omitted Webster's second case (*Gyn. Trans.*, 1907, xxxii, 122) that was beautifully mounted and exhibited at the meeting of the American Gynecological Society in 1907. Webster is the only one to exhibit two specimens of this condition, and that they should occur within three years in one small town is quite remarkable. Norris and Mitchell state the specimen they report fulfils all the criteria Spiegel-

berg formulated in 1878. They are: (1) The tube on the infected side must be intact and have no organic connection with the gestation sac; (2) the foetal sac must occupy the position of the ovary; (3) it must be connected with the uterus by the ovarian ligament; and (4) definite ovarian tissue must be found in the sac wall in several places.

**Fifty Cases of Pfannenstiel's Transverse Abdominal Incision.**—A. HELSTED (*Zentrbl. f. Gynäk.*, 1908, xxii, 248), during a period of three and one-half years, has made use of Pfannenstiel's transverse incision in 50 cases. The operations performed included ventrofixation, salpingo-oöphorectomy, myomectomy, supravaginal hysterectomy, and panhysterectomy (including four Wertheim operations). The largest fibroid removed was the size of a child's head and the largest ovarian tumor extended to the umbilicus. The incision was often 15 cm. in length; 38 of the patients were examined six months or more after the operation and the cosmetic results in all cases were excellent. There was no indication of a hernia or separation of the recti muscles. One patient was confined one and one-half years after the operation and one six months after with no bad results. According to Helsted's experience, Pfannenstiel's incision may be used with good results in the Wertheim operation and for the removal of ovarian tumors if the cyst is punctured. It is not suitable in suppurative or tuberculous cases. It is believed to have important advantages over the median incision in many cases.

**One Hundred and One Consecutive Hysterectomies for Fibroids Attended with Recovery.**—J. BLAND SUTTON (*Jour. Obstet. and Gyn. Brit. Emp.*, 1908, xiii, 328) reports this series of cases with verification by others and subsequent reports upon 90 per cent. of them. Total hysterectomy was performed in 7 of the cases. The ages were: under thirty years, 5 patients; under forty years, 33; under 50 years, 47; above fifty years, 16. In 1 Sutton found cancer of the corporeal endometrium and in 1 the ureter was injured and later the corresponding kidney sacrificed. These operations were performed during the years 1906 and 1907 in the Middlesex Hospital and the Chelsea Hospital for Women. The statistics presented demonstrate that Sutton has reached an irreducible minimum in mortality.

**Diffuse Adenoma of the Cervix of the Uterus Simulating Cancer.**—HARTMANN and LECENE (*Ann. de gyn. et d'obst.*, 1908, v, 297) report a case of this kind that occurred in a woman, aged forty-seven years, who had had for twelve years a malodorous discharge and considerable metrorrhagia. She was married at the age of twenty years and the last of her four children was born at the age of twenty-five years. An examination revealed in the place of the cervix a rounded, ulcerated, irregular, bloody tumor, that was considered carcinoma. The ulceration occupied all the portio vaginalis and involved the vaginal fornices; the broad ligaments appeared to be normal. Abdominal hysterectomy with resection of the vagina was performed successfully. A microscopic examination showed the cervical mucosa had been supplanted by vegetation and the muscular tissue was not abnormal. Large hypertrophied glands occupied the most of the cervix, but not the infiltration



as noted in epithelioma. The active portion of the neoplasm was formed from a large number of pseudoglandular cavities having a lining of non-ciliated cylindrical epithelium resembling very closely in structure the normal cervical glands. The pseudoglandular cavities were well closed, but no tendency to epithelial infiltration of adjacent tissue was found, nor was epithelial proliferation of the spaces apparently very active. The diagnosis finally made was diffuse adenoma of the cervical mucosa developed from the deep portions of the mucous glands. A thorough literary research led to the conclusion that this is the third case of the kind to be recorded.

**Second Report on Operations for the Relief of Pelvic Diseases of Insane Women, Including 411 Patients.**—LE ROY BROWN (*Amer. Jour. Obst.*, 1908, lviii, 87) reports the results of operations on 411 patients in the Manhattan State Hospital for the Insane, during the last five years. Of these 72 were discharged as recovered, 32 of whom showed a much increased rapidity of improvement after operation. No patient is included in this number whose mental progress was not strikingly marked after the operation in comparison with her progress before the operation was done. 12 of the 32 abdominal operations were done for the following conditions: 3 subtotal panhysterectomies for fibromyoma uteri; 7 uterine suspensions, in 2 of which one appendage was removed; in 1 of them gastroplication was added; in 2 of them small fibromyomas were also removed; 1 was done for removal of an ovarian cyst; 1 was a herniotomy for inguinal hernia. The other 20 cases had plastic operations for endometritis, lacerated cervix, lacerated perineum, and displaced uterus. In but 3 of 37 cases of double appendage ablation did apparent marked mental improvement follow, which tends to demonstrate that pathological conditions of ovaries are not such important etiological factors as is generally thought. Of the 32 improved cases 25 had the dominating symptom of depression and were classified prior to 1904 as melancholia, acute and chronic, involution melancholia, and depressive hallucinosis. In the new-hospital classification they fall under the heading of maniac-depressive insanity, and the involution period of life; 5 were patients in an excited or exalted mental state. The remaining 2 had dementia præcox and paranoic symptoms. The importance of early operation and treatment is indicated by the proportional improvement, it being for the first six months of insanity, 58 per cent.; for the second six months, 33 per cent.; for the third six months, 26 per cent. Brown states, owing to the evident complexity of the etiology which exists, even in the best circumscribed symptomatic groups, it is clear that in the general estimation of the value of surgical interference, it must be regarded as a procedure ranking with our other therapeutic measures which aim to get the patient as quickly as possible into a condition of bodily comfort and physical vigor. Manic-depressive insanity is regarded rather as a disorder arising on a constitutional basis and expressing itself in one or more attacks liable to be elicited by a great variety of causes, among which states of physical ill health are very important. In cases in which the surgeon can relieve the condition which is wearing on the patient, causing worry, pain, or loss of sleep, good results may be expected to follow, and sometimes recurrence of attacks prevented. In the infective exhaustive group good results can be expected wherever

foci of infection can be attacked and removed, or where any exhausting influence can be checked.

**Perineorrhaphy for Complete Lacerations.**—T. J. WATKINS (*Surg., Gyn., and Obst.*, 1908, vii, 1) reviews the history of principles evolved in perineal repair and then describes a plan he has adopted in 5 cases and which is a slight modification of the J. Collins Warren operation. It materially lessens risk of infection from the rectum and anus. The illustrations are unusually clear and leave little necessity for text. The method affords an impermeable mucous covering for the sutured ends of the term sphincter ani muscle.

## OTOLOGY.

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**Experimental Investigation of the Resistance of the Drum-head.**—ZALENSKI (*Ztschr. f. Ohrenheilk.*, 1907, lii, 76). The material employed by Zalenski in determining the resisting power of the drum-head to increasing atmospheric pressure in the external canal consisted of 232 fresh human cadavers and 10 dogs. The results were as follows: The normal drum-head ruptured in 65.76 per cent. of the cases under a pressure of from 77 to 152 c.c. of mercury, or 1 to 2 atmospheres; in 23.4 per cent. there was a resistance to over 2 atmospheres, and in 10.8 per cent. there was rupture at a pressure of less than 1 atmosphere. The greatest pressure sustained before rupture was that of 228 c.c., or about 5 atmospheres, and the least that of 28 c.c. Cicatrices, thinning of the drum-head, and the sequences of inflammatory processes caused a decrease of the resisting power to 22.08, 42.83, and 78.55 c.c. respectively; connective tissue thickening increased the resistance to 160.3 c.c., while in cases of calcareous deposit the resisting power was still further increased. With advance in age, the resisting power of the drum-head steadily decreases, being greatest in the new-born and up to the tenth year. The incident ruptures occurred almost uniformly in the pars tensa, rarely in the pars flaccida, usually single, rarely double, and following the line of the manubrium across the drum-head, but without completely reaching the periphery. The ruptures resulting from high pressure were usually more extensive than those resulting from low pressure, and were more common in the anterior than in the posterior segment.

**The Influence of Continued Use of the Telephone.**—BLEGVAD (*Archiv. f. Ohrenheil.*, 1907, lxxii). The conclusions arrived at by Blegvad, in a series of precisely conducted observations, embodied in an extended record beyond the capacity of a brief review but well repaying careful reading, are as follows: In 26.4 per cent of the 371 telephone operators,

with normal hearing, who were made the subject of examination, there was a retraction of the drum-head in the ear to which the receiving instrument was usually applied, the other ear evidencing either none, or only a slight retraction. The continued use of the telephone caused no depreciation of the hearing in operators with normal ears, nor was there on the other hand, any appreciable increase in the capacity for the hearing of tones of high pitch and slight intensity, as is sometimes claimed by the operators, this claim being supported rather by the increase in the accommodative power for tones of this class and by the gradually acquired habit of eliminating, mentally, the co-incident and the extraneous noises. The aural lesions and traumatic neuroses incident to the accidental introduction upon the telephone line of strong currents are the result of the exhibition of a loud and sudden sound and are to be guarded against by proper protective construction in the telephone lines.

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**Isolated Primary Tuberculosis of the Lobule.**—PAETZOLD (*Ztschr. f. Chir.*, 1907, lxxxiv, 469). In three subjects, aged respectively fourteen, fifteen, and twenty-four years, the affected lobule was swollen and thickened, the skin on both anterior and posterior surfaces being shining, of a bluish red color, but free from nodules or ulceration, and the affected area sharply delimited from the surrounding healthy skin; all of the patients wore earrings. The examination of excised portions showed areas of necrosis and giant cells. The author concludes that the isolated primary disease of the lobule in these cases was the result of a tuberculous infection with primary tuberculosis of the subcutaneous fatty tissue, the point of entrance being the punctured opening for the earring, the remaining portions of the auricle being free from infection. The disease is of slow progress and its treatment consists in the radical excision of all the affected tissues.

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## PATHOLOGY AND BACTERIOLOGY.

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**The Hematology of Carbon Monoxide Poisoning.**—It is known that carbon monoxide has an affinity for the hemoglobin of the blood about 140 times greater than oxygen; and that it acts as a poison by throwing out of commission the hemoglobin of the blood as an oxygen carrier, and thereby preventing normal oxidation of the tissues.

Nasmith and Graham (*Jour. Physiology*, 1908, xxxv, 32) have made an interesting study of the blood of guinea-pigs during acute and chronic carbon monoxide poisoning. Guinea-pigs were kept in an atmosphere

which contained sufficient carbon monoxide to saturate 25 per cent. of the hemoglobin. The animals soon became acclimated, gained weight, appeared active and happy, and lived for fifteen months. Soon after the animals are put into this atmosphere a change becomes manifest in the hemoglobin percentage, and the number of red blood corpuscles. There is a gradual increase in the percentage of hemoglobin and in the number of red blood corpuscles. Guinea-pigs, whose normal hemoglobin content was 88 per cent. showed an increase to 105, while the red blood corpuscles rose from 6,000,000 to about 8,000,000. A gradual increase in the hemoglobin saturation up to 45 per cent. brought about even more marked changes. The red blood corpuscles almost doubled their number, rising to 10,000,000, and the hemoglobin reached 109 to 110. Soon after the guinea-pigs are introduced into carbon monoxide atmosphere sufficient to saturate 25 per cent. of the hemoglobin, the red blood cells show degenerations, and many erythroblasts appear. When the animals are kept again in the air, after living for months in the carbon monoxide atmosphere, the red blood corpuscles and hemoglobin gradually decrease to their normal proportions. If guinea-pigs are placed in an atmosphere of CO which causes 45 per cent. hemoglobin saturation, they usually die within a few days. The blood changes just described are considered to be analogous to those observed in human beings and animals at high altitudes. Not only are the red blood corpuscles and hemoglobin altered, but the white cells are also affected. In acute CO poisoning there is a marked and rapid leukocytosis with increase in the numbers of pseudo-eosinophiles, and decrease in the lymphocytes. The eosinophiles also undergo interesting changes. There is at first an increase followed by a marked decrease with the appearance of eosinophilic myelocytes. All of these blood changes are referable to an intoxication, not by the CO itself, but by certain tissue products which it is impossible for the animal to oxidize to harmless substances, since the normal amount of oxygen carried to the tissues by the red blood corpuscles is substituted by the inert substance, carbon monoxide.

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**The Pathogenesis of Gallstones.**—In 1905 Gerard first showed that when artificial media, which contained both bile acid salts and cholesterolin, was inoculated with colon and typhoid bacilli, the cholesterolin was precipitated from the solution. Kramer later demonstrated the same phenomenon by using a mixture of bile and bouillon. EXNER and HEYROVSKY (*Wein. klin. Woch.*, 1908, xxi, 214) have added some interesting observations to this subject. They have confirmed the experiments of Gerard and Kramer, and find further that when bile is inoculated with colon bacilli a large proportion of the bile acid salts are decomposed. This was found true, as could be established by chemical analysis, for the filtered and sterilized bile of ox and man, as well as for a solution of sodium taurocholate and glycocholate in nutrient broth. It is well known that cholesterolin is soluble in an aqueous solution of bile salts, but Exner and Heyrovsky found that only half as much cholesterolin was dissolved in a 0.5 per cent. solution of the sodium bile salts as in a 1 per cent. solution. They, therefore, concluded that the precipitation of cholesterolin from the bile inoculated with colon and typhoid bacilli, is due to the fact that so much of the bile acid salts are destroyed that the entire amount of the cholesterolin can-

not be held in solution. They further show that the action of different bacteria varies greatly as regards this property of destroying the bile salts. The typhoid bacillus possesses it to a great degree, whereas streptococci have little or no affect.

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**Granulation of the Red Blood Corpuscles in Anemic Conditions.**—ASKANAZY (*Ztschr. f. klin. Med.*, 1907, lxiv, 288) has been able to find red blood cells containing the basophilic granules, so typical of lead poisoning, in a variety of anemic states. He has found them in the blood from cases of pernicious anemia, various forms of secondary anemia, in chlorosis, and in lead poisoning. He considers that these granules are the same as the ones described by Plehn in malaria. The granules are present in red cells which show polychromatophilia and he thinks, moreover, that all granulated cells show some degree of polychromatophilia. The cells which present the greatest polychromatophilia have the finest granules, whereas, the cells with coarse granules show but slight polychromatophilia. The two conditions he considers are stages of the same process which represents not a degeneration of the cells, but is evidence of regeneration. This conclusion he arrives at after some study and experimentation. Askanazy could not find granular cells either in the blood or bone marrow of normal adults, of the newborn, or of foetuses. In the blood of the newborn and foetus normoblasts, a few megoblasts, and polychromatophilic cells were seen. In animals the results were somewhat different. Granular cells were often found in the blood of healthy rabbits, and were constantly present in the blood of mice embryos. Four days after bleeding rabbits granular cells appeared in the circulation together with polychromatophilic cells and normoblasts. Rabbits injected with lead acetate showed great numbers of nucleated red cells, polychromatophilic and granular cells in the circulation, but except in one or two instances, when granular normoblasts were seen, granular red cells were not found in the bone marrow. Askanazy believes that in man, at least, the granulated red cells do not appear in the blood under normal conditions. The curious fact that the granulated cells are found only in the circulating blood and not in the bone marrow, is dependent upon the action upon the unripe red cells of the blood serum, which disease has modified in some way

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**The Etiology and Epidemiology of Plague.**—(A summary of the work of the Plague Commission, issued under the authority of the Government of India by the Sanitary Commissioner with the Governments of India, Simla, Calcutta, 1908.) The important conclusions and results of the investigation of the commission, which has been working upon this problem for over two years, are that pneumonic plague is highly contagious, although fortunately it is rare, and since it forms only about 3 per cent. of all cases plays a very small part in the general spread of the disease. Bubonic plague in man is entirely dependent upon the disease in the rat. From the rat the infection is conveyed to man solely by means of the rat flea, which, of course, spreads the infection among the rats themselves. It was found that a large majority of the plague cases occur singly in houses, and that where

more than one case occurred in a single house the attacks were generally simultaneous. Plague is usually conveyed from place to place by imported rat fleas, which are carried by people on their persons or in their luggage. The human agent, not infrequently, himself escapes infection. Unsanitary conditions have no relation to the occurrence of plague, except in so far as they favor infection by rats. The non-epidemic season is bridged over by acute plague in the rat, accompanied by a few cases among human beings.

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**The Bacteriolytic Property of Lecithin.**—BARSENGE (*Deut. med. Woch.*, 1908, xxxiv, 139) has found that lecithin has, in vitro, a marked bacteriolytic effect upon typhoid bacilli. The lecithin was used in 1 per cent., 0.1 per cent. and 0.01 per cent. aqueous emulsions. When large quantities of a culture of typhoid bacilli were brought in contact with the 1 per cent. emulsion, the bacilli showed such fragmentation and degeneration that the picture simulated very closely that seen in the Pfeiffer phenomenon. Cultures showed that 1 per cent. emulsions of lecithin, when inoculated with typhoid bacilli and incubated, were sterile. A very preceptible inhibition of growth took place in 1 to 1000 emulsions, while the growth in 1 to 10,000 emulsions was practically the same as in the control bouillon tubes. The hope that animals might be made refractory to inoculations of typhoid bacilli by previous injections of lecithin emulsions proved unfounded. Animals inoculated with many times the fatal dose of typhoid bacilli in lecithin emulsions succumbed as rapidly as the control animals. It was, however, found possible to obtain a toxin, in the case of typhoid bacilli an endotoxin, by treating the bacteria with lecithin and chloroform. With this toxin animals could rapidly be immunized against many times the fatal dose of living typhoid bacilli.

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**Blood Formation in the Spleen and Liver in Experimental Anemia.**—DOMARNS (*Archiv. f. exp. Path. u. Pharmacol.*, 1908, lviii, 319) has demonstrated that changes in the spleen and liver, similar to those described by Meyer and Heinecke in man in pernicious anemia and in other severe anemias, may be produced in animals by the administration of hemolytic substances; his results confirm those obtained by Morris. In some instances, especially in chronic anemias with regeneration, the liver and spleen both resembled the organs of the embryo at the stage when these organs are engaged in hematopoiesis. The changes produced are looked upon as compensatory regenerative efforts of the organism.

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THE  
AMERICAN JOURNAL  
OF THE MEDICAL SCIENCES.

NOVEMBER, 1908.

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ORIGINAL ARTICLES.

**GALLSTONE DISEASE.<sup>1</sup>**

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WHILE, of late years, much consideration has been given to the subject of gallstone disease, and while many brilliant cures have been brought about by the proper application of surgical methods, the last word on the subject has yet to be written, and there are many moot points of equal interest to the internist and the surgeon that impress me with the importance of further discussion of disease of the biliary tract. By reason of its function as the excretory apparatus of the largest gland in the body, by reason of its intimate relations with vital organs in the upper abdomen, and by reason of its liability to infection and its commanding position to spread infection over a greater or less extent of the peritoneal cavity, the biliary apparatus may justly be considered unique.

To many surgeons the biliary apparatus consists, surgically speaking, of the hepatic ducts, the gall-bladder, the cystic duct, and the common duct; but studies in the pathology of the living have impressed me with the importance of considering the extent of the biliary tract from its developmental standpoint. Thus, every secreting cell in the liver is surrounded on one or more sides by a bile capillary; these capillaries unite to form bile vessels situated between the lobules of the liver; the bile vessels, increasing in size, unite with one another until eventually the large common hepatic duct is formed, and this, uniting with the cystic duct from the gall-

<sup>1</sup> Read at the Forty-first Annual Meeting of the Canadian Medical Association, Ottawa, June 11, 1908.

bladder, forms the common bile duct. But not only developmentally, but also clinically, the biliary tract does not end here. Embryologically the pancreas with its main duct and intermediate tubules is derived from the outgrowth of the biliary tract from the duodenum, and clinically this abdominal salivary gland is frequently secondarily involved in gallstone disease. Hence, considered in this wise, there is a very extensive area comprising countless square inches, which, like the mucous membrane of the respiratory and the urinary systems, affords a broad and fertile field for the implantation and unlimited spread of infection.

The common infectious agents of the biliary tract, in order of their frequency, are: *Bacillus coli communis*, *Bacillus typhosus*, and the common pyogenic organisms. How do these bodies invade the biliary tract? The three ordinary pathways are the portal circulation, the common bile duct, and the systemic circulation.

What is the immediate result of infection of the biliary tract? "As in other mucous canals . . . the production of a catarrh, with the usual inflammatory phenomena—oedema and congestion of the mucous membrane, increased production of mucus, and desquamation of epithelium. If the biliary circulation is free and unimpeded the results of this catarrh are washed away for the most part, but on account of special local conditions (largely dynamic) they are likely to accumulate, to become accentuated, and to persist in the gall-bladder. In the event of obstruction to the free flow of bile these are the more certain to occur. In many cases the lesions thus provoked are entirely latent or unannounced by noteworthy or unequivocal symptoms; they may pursue a short course, or they may continue for years; and they are one of the most important factors, in fact the important factor, in the etiology of gallstones.

"This infection of the biliary tract is of the utmost significance, and forms an integral part of what is commonly designated calculous cholecystitis and cholangitis. The phenomena may develop: (1) Acutely, without preceding clinical signs referable to the gall-bladder; (2) subacutely; and (3) chronically. The ensuing pathological lesions are of the greatest diversity: Thus, for instance, gallstones may or may not be present, and the concomitant inflammatory phenomena may be of varying grades—from the mildest catarrhal lesions to widespread phlegmonous and ulcerative processes that may lead to perforation or gangrene of the gall-bladder; gallstones, if present, may be quiescent or active; they may be present in the gall-bladder, or in any one of the ducts, or in all the ducts, or in the ducts and not in the gall-bladder; they may cause an acute or chronic, partial or complete, temporary or permanent, obstruction of the cystic, the hepatic, or the common bile ducts, and, on the other hand, such obstruction may occur in the absence of gallstones (being due to swelling of the mucous membrane, kinking of the ducts, or obstruction from without), and in the presence of gallstones the ducts

may be partially or completely patulous; the gall-bladder may be distended or contracted, its walls thinned or much thickened, and its lumen ultimately may become almost if not quite obliterated; it may contain bile, mucus, blood, or pus, or combinations of these, in addition to or in the absence of gallstones; adhesions may form between the gall-bladder and adjacent structures (the liver, the stomach, the duodenum, the colon, the omentum, etc.), and by way of the adhesions the gallstones may rupture into the gastro-intestinal tract and sometimes cause intestinal obstruction; or purulent pericholecystitis and pericholangitis, localized or generalized peritonitis, pylephlebitis, pericholangitic abscesses of the liver, fistulæ, acute and chronic pancreatitis, etc., may ensue; and, finally, in some cases a general bacterial, often pyococcic, infection, with or without multiple abscess, may develop."<sup>2</sup> Furthermore, the long-continued infection may seriously involve the arterial and urinary systems, producing such degeneration of the myocardium and kidneys that often makes the surgeon loath to operate.

Cholecystitis may be calculous or non-calculous. The larger one's experience in gallstone disease the less able is he to state whether gallstones are, or are not, associated with cholecystitis. Cholecystitis is caused by invasion of the fertile mucous membrane of the gall-bladder by pathogenic bacteria. This event brings about the classical symptoms of inflammation. Pain is situated in the epigastric region, is usually sharp, appears suddenly or gradually, and is increased by motion either of the entire body or of regional organs, such as the stomach in peristalsis or in vomiting. The accompanying tenderness indicates the situation of the gall-bladder in the absence of peritonitis; the presence and extent of peritoneal irritation or peritonitis is indicated by the extent of the associated tenderness. The swelling of the mucous membrane occludes the cystic duct, and thus isolates the gall-bladder from the intestine. By loss of function the gall-bladder, instead of being the reservoir for bile, now becomes the repository of pathological exudates. This causes distention of the organ, and thus the tumor may, in favorable cases, be palpated. In the case of the gall-bladder, loss of function bears much significance, as the products of inflammation may lead to the formation of gallstones.

The severity of the cholecystitis is indicated by the general symptoms, and varies with the virulence of the infection; for example the simple pathological processes of oedema and congestion of the mucous membrane, increased production of mucus, and desquamation of epithelium unite to form the clinical entity of acute catarrhal cholecystitis. This entity makes itself known to the outside world by the general symptoms of fever with its accompanying

<sup>2</sup> A. O. J. Kelly: Infections of the Biliary Tract. AMER. JOUR. MED. SCI., 1906, XXXII, 446.

phenomena of chill, accelerated pulse, vomiting, dry and coated tongue, scanty high-colored urine, and leukocytosis. Locally, there is pain, tenderness, and rigidity. Such a mild case I consider appropriate for judicious medical treatment, for if the biliary circulation is free and unimpeded the results of this catarrh are washed away for the most part. If this mild cholecystitis yields promptly to medical treatment, and the patient is having his first attack, I think operation may well be postponed until further symptoms arise. Calculi are probably absent in such mild cases in early attacks, and such patients seem to me particularly suited for the so-called Carlsbad cure. When the attacks of cholecystitis are repeated, and especially when discomfort persists in the intervals, operation is demanded to obtain a cure. The frequency with which mild but recurrent attacks of cholecystitis give rise to pericystic and pyloric adhesions, I fear, is not duly appreciated by all of the profession.

But suppose the medical attendant does not see the mild case clear up, that the symptoms become more severe: what is going on in the gall-bladder? There is obstruction to the free flow of bile, and as Dr. Kelly says because of special local conditions (largely dynamic) the results of the catarrh accumulate, become accentuated, and accumulate in the gall-bladder. Here the infection is more virulent, and the pathological changes have now produced the clinical entity of acute purulent cholecystitis, or empyema, a condition which I found in 16.4 per cent. of a series of 182 cases recently operated upon. The fever now becomes hectic in type, and the brow is bathed in sweat; there may be delirium of the low, muttering type. Local pain, tenderness, and rigidity, are increased. The patient loses flesh, his appetite is poor, and he frequently asks for water to drink. Here medical means are futile, but a cure is usually effected by cholecystostomy, during which procedure any obstruction that may be found in the cystic duct should be removed. Empyema requires cholecystectomy only when of long standing, such chronicity resulting in irreparable disease of the walls of the gall-bladder.

If the infection be very virulent, the walls of the gall-bladder will become infiltrated by the products of phlegmonous inflammation, which may undermine the mucous membrane, interfere with the blood supply of the organ, and lead to gangrene. Other varieties of acute cholecystitis, of pathological interest, are the hemorrhagic and the ulcerative. The hemorrhagic form is made manifest, when, upon opening the gall-bladder, blood clots are found. In this instance microscopic ulcerations are active in opening into congested veins, and it is possible that, for a time, at least, the bleeding is furthered by the local anti-clotting action of the bile, an action that, to the annoyance of the surgeon, is most manifest in that state known as *cholemia*. Ulcerative cholecystitis becomes of interest clinically when it results in perforation of the gall-bladder. Gangrene of the gall-bladder naturally requires excision of the gall-bladder, and also does per-

foration, since it occurs most frequently when the gall-bladder walls are extensively diseased.

If unchecked by surgical means the infection may spread from the gall-bladder through the cystic and hepatic ducts into the interlobular bile vessels, and even into the intercellular bile capillaries. Such a pathological extension creates the clinical entity of infectious cholangitis, the symptoms of which are manifested by ague-like attacks, to which Charcot has applied the term of intermittent hepatic fever. To the previous symptoms of cholecystitis there is now added the sign jaundice, which may be of the intermittent type. But it must be remembered that infectious cholangitis often follows upon the impaction of a calculus in the common bile duct. The treatment of this condition is to see that the entire biliary tract is clear and unobstructed, and to secure free drainage.

If unrelieved acute infectious cholangitis may be the forerunner of suppurative cholangitis. Suppurative cholangitis may also arise from acute infectious disease, especially typhoid fever and influenza, from carcinoma of the bile ducts, and from hydatid disease. Symptoms of septic fever, rapid loss of flesh, and obstinate jaundice now supervene. The treatment is that of infectious cholangitis, namely, bile drainage.

Acute purulent hepatitis is the terminal condition of this triumphal march of bacteria from the gall-bladder to the liver. In this organ, wrecked by infection, the last stand of the organism is made: multiple hepatic abscesses form, and the patient finally succumbs from the uncontrollable fever and toxemia. It is in such cases that operation retards the progress of modern surgery. If the infection be less virulent, biliary cirrhosis of the liver, usually the result of gallstone blockage, may ensue. In the presence of this latter entity, clearance and drainage of the biliary tract may relieve the patient by depleting the liver, but it cannot remove the adventitious fibrous hypertrophy.

Having traced infection of the biliary tract by continuity let me trace it by contiguity. It is here that a gall-bladder, its walls permeated by phlegmonous infiltration, becomes a paramount source of danger by reason of its commanding position to spread infection over a greater or less extent of the peritoneal cavity, a circumstance to which attention was directed in the early part of this paper. The virulent bacteria may pass directly through the gall-bladder walls, or give rise to ulceration or perforation, and then quickly involve the neighboring peritoneum. If the peritoneum be alert, pericholecystic abscess may ensue, with marked tenderness and rigidity; a correct diagnosis of this condition should lead to immediate evacuation. In neglected cases the pus, like water, follows in the direction of least resistance, and this may lead it into the peritoneal cavity, the alimentary tube, the subhepatic retroperitoneal tissue, or, if it accumulate between the superior surface of the liver and the right cupola of the diaphragm, it may creep through this into the right pleural

sac and the lung, to be spat up by the patient. Much more commonly than this, however (in 58.7 per cent. of 182 cases recently reported by me), the diffusion of the toxins in the regional peritoneum in small repeated doses, evokes patches of fibrinoplastic exudate, which reach out octopus-like for nearby organs, and, by subsequent contraction, throttle more or less completely those that are hollow, as the stomach, duodenum, or colon, thus increasing the complaint of the patient and the operative difficulty of the surgeon. The omentum, the organ of phagocytosis, may complete the Gordian knot by fettering the already shackled tissues to the liver; the frequency with which such masses are mistaken for malignant disease is attested by operators. However, until this tangle of tissue is established, the patient's life probably hangs in the balance, for such a mass of adhesions may represent the only alternative to diffuse purulent peritonitis.

A gall-bladder once damaged by infection may, if the infection be mild, undergo complete resolution. Repeated mild attacks of inflammation, or a severe and extensive infection may determine chronic cholecystitis. Interference with the physiological periodic expulsion of bile from the gall-bladder—a condition brought about by permanent obstruction of the cystic duct from chronic inflammatory changes, or by a stone—results in absorption of the bile contained therein at the time of blockage, and its replacement by clear, watery mucus. Thus hydrops of the gall-bladder occurred in 7.1 per cent. of 182 cases recently reported by me. This condition is one of the few that calls for cholecystectomy, since obliteration of the cystic duct renders the gall-bladder not only useless, but also a continued menace from the liability to reinfection or even of rupture. The only exception I would make to this rule is obstruction of the cystic duct by stone, if recent; if the gall-bladder show but little macroscopic evidence of disease, and if after dislodgement of the stone bile flows immediately into the gall-bladder, it may be wise to leave the organ. Destructive bacterial invasion of the walls of the gall-bladder is followed by the ultimately destructive effects of constructive repair, resulting in abolition of the normal suppleness of this little bile-containing bulb. Contraction, that inevitable consequence of fibrous degeneration, gradually obliterates the cavity of the gall-bladder, and the surgeon sees frequent instances in which this has been accomplished. What space may remain in such an organ is usually filled with ropy, tarry, inspissated, and pathologically altered bile. Such shriveled gall-bladders should be drained or removed, in keeping with the possibilities of the case and the judgment of the operator.

In order to emphasize these remarks by practical illustrations, I have analyzed the 72 cases of gallstone disease operated upon by me during the twelve months ending with April 1, 1908.<sup>a</sup> Of the

<sup>a</sup> For a larger list of 217 cases previously operated upon by me, see *AMER. JOUR. MED. SCI.*, 1908, *xxxv*, 137.



72 cases, 9 were examples of chronic, non-calculous cholecystitis, with no mortality; whilst of the remaining 63 cases of cholelithiasis, 4 were fatal.

Glancing over the histories of the 9 sufferers from non-calculous cholecystitis, I am impressed with the constancy of symptoms of dyspepsia, and the presence of adhesions. Thus, 7 of the 9 complained of such discomfort after eating, as oppression in the stomach, burning, and eructations of gas. And in 8 of the 9 cases adhesions were found, usually between the gall-bladder and some part of the alimentary tube, as the stomach, the duodenum, or transverse colon, or between the gall-bladder and omentum. These adhesions are relics of bygone infection, and make dyspeptics of their bearers. That the infection, as a rule, had long since departed was shown by positive cultures being obtained from only 2 of the 9 cases, while in 2 others there were no bacteria, but lymph nodes were enlarged, in one case along the cystic, and in another along the common duct. Furthermore these patients were subject to frequent attacks which increased in number with the duration of the disease. Such attacks usually followed dietary indiscretions, and started with pain in the right hypochondrium, radiating to the back and right shoulder blade, with nausea and vomiting, sometimes chills and fever, and sometimes followed by jaundice. Some patients complained of continuous tenderness over the gall-bladder, frequently aggravated by exercise—further evidences of the baneful effect of adhesions. The gall-bladders were usually atrophied, with walls thickened sometimes to as much as one-quarter of an inch. One patient had been operated upon two years previously, when 200 stones were removed from the gall-bladder. Within the past year he had three attacks of paroxysmal, crampy pain in the epigastrium, referred to the right scapula, preceded by chills and followed by gaseous eructations and vomiting. Operation revealed a greatly thickened gall-bladder, firmly adherent to the anterior abdominal wall. This gall-bladder was removed. Of the 9 cases I was able to save the gall-bladder in 6, which were merely drained; the remaining 3 were so badly diseased as to demand removal.

While cholecystitis in its various forms may be present without cholelithiasis, yet the two are so frequently wedded etiologically and pathologically that it is not strange that a differential diagnosis cannot always be made by clinical signs alone. The natural history of gallstones is interesting; their accurate diagnosis, satisfying; their removal, comforting.

Normal bile has been found contaminated with bacteria, but this is of little moment so long as there is no disease of the gall-bladder walls, and the biliary stream is unimpeded. Obstruction to the outflow of bile from this bulb, therefore, is the first step toward calculus formation, since whenever bacteria are bottled up they tend to create mischief, although now and then they die out.

Infection is the forerunner of inflammation; inflammation means cell proliferation, exudation, and altered function—a succession of events favorable to the precipitation of biliary salts. By means of mucin these salts are agglutinated, and with the cholesterin formed by degenerative changes in the epithelial cells, form calculi. At first the stones are soft, but, with time, become harder and harder. Recent soft calculi are preferred by bacteria to older, harder ones; for, whereas bacteria are continually present in the former, they are frequently absent from the latter. In a recent article on the etiology of cholelithiasis, Funke says: "While the almost constant presence of bacteria in recently formed calculi appears to indicate their presence in the bile at the time of the calculus formation, the experiments of Gilbert and Fournier and of Chauffard furnish sufficient ground to refute such conclusion. These investigators have succeeded in demonstrating secondary penetration of the calculi. They also succeeded in demonstrating that the organisms travel in the other direction. These observations may explain the frequency with which soft calculi are inhabited by organisms. The finding of sterile bile and infected calculi at the same operation can scarcely be held to controvert secondary penetration, for the bile may have become bacteria free after having infected the concretions. Although secondary penetration cannot be doubted in the light of the experiments quoted, yet there are few authors who hold that the presence of bacteria in the concretions must in all instances be regarded as such."

Without discussing further how gallstones become infected with bacteria, the fact remains that such bacterial hives argue ill for their bearer. Once formed, how long before gallstones produce wailing and gnashing of teeth? Richardson says: "During that more prolonged period of time between the first aggregation of the crystals which form the gallstone and the development of a gallstone large enough to obstruct the duct, a very considerable interval of time must elapse. Just how long that period of time may be is a matter of inference. Before they begin to offend, gallstones usually have a very considerable age. The age of a stone is judged not by its size, but by its consistency. A soft stone, easily crushed between the fingers, of a light lemon color, I usually regard as a recent one. A dark, rough stone, especially if it is made up of different kinds of salts varying in color and in hardness, would probably be much older than a stone composed of salts of the same consistency and the same color."

I believe there is scarcely anyone with large experience in gall-bladder surgery who does not see examples of the different stages through which gallstones pass during their development, did he but recognize them as such. In discussing the pathology of cholecystitis, McFarland says: "Sometimes gall-bladders are found filled with inspissated bile, rich in bacteria, sometimes filled with bile containing

a pulpy mass, probably a precipitate of the bile salts about this bacteria mass; sometimes the entire contents of the organ will be pasty, mushy, gritty, or gravelly; sometimes a single stone and sometimes a large number of stones will be present."

From the above remarks I think I am justified in bringing up the question of the preventive treatment of cholelithiasis. This, however, seems premature at the present time, since the early symptoms of even fully matured gallstones are just beginning to be understood and are not always detected; the symptoms that may be interpreted as forerunners of those of fully formed calculi are even less known.

More significance, I think, must be attached to the contents of opened gall-bladders. When a surgeon drains a gall-bladder of the products of cholecystitis; when he empties it of inspissated bile rich in bacteria, or of bile containing a pulpy mass; or when he evacuates pasty, mushy, gritty, or gravelly material, is he, with his knowledge of the natural history of gallstones, not justified in believing that in each of these instances he has carried out the preventive treatment of cholelithiasis? When he removes stones, since these are found after an unknown, but probably long lapse of time, he is operating comparatively late in the disease. And when he must perform choledochotomy for calculi that have reached as far as the common duct, or when he drains a gall-bladder for chronic pancreatitis that has resulted from gallstone disease, or removes tissue made cancerous by the same cause, he may find consolation in the old saying, "Better late than never."

Gallstones lodged in the fundus of the gall-bladder may be likened to shot in the breech of a gun, and the biliary ducts to the barrel of the gun. If the gallstones remain quiescent, as is claimed for them in a certain percentage of cases, the gun is never discharged. If, on the other hand, infection or some other factor starts the gallstone or stones along the biliary tract, the gun is discharged and the explosion manifests itself in the colicky pains and other disturbances the patient experiences. The missile or gallstone may travel *per vias naturales*, and drop harmlessly out of the anus, or be vomited forth. Or, by ulcerating a passage for itself, it has the effect of a gunshot wound from a missile of extremely low velocity, and makes its way by fistulæ directly to the surface, or into the digestive tube, or elsewhere.

It is doubtful if gallstones can be present without producing symptoms, as is claimed for about 5 per cent. of gallstone subjects. We now know that it is not necessary for a diagnosis that the manifestations of gallstone disease be displayed on transparencies bearing, in large letters, the words "colic" and "jaundice." We look to the earlier writings of the disease, and attach due significance to the various expressions of "indigestion," as epigastric distress, anorexia, flatulence, eructations, heart burn, nausea, and vomiting. If there is not out-and-out pain, there may be, as Richardson says, a consciousness of discomfort in the epigastrium, in the right hypochondrium, or some-

times in the left—"a discomfort for which the patient seeks some simple remedy which she has in the past found efficacious—a hot water bottle, a liniment, an aromatic, a digestive, a carminative." In such cases pericholecystic adhesions or gallstones provoke these slight symptoms. Richardson writes: "One patient examined very recently, who has a gall-bladder filled by two large stones, says that she has never had any trouble, but she goes on to say: 'Of course I have to be very careful what I eat on account of these bilious attacks which I have been subject to for years.'" Thus, not only must the patient restrict his appetite, a matter which means mental suffering even for the healthy, but he must suffer the consequences of dread of eating, which, continued for a long time, brings loss of weight and strength, and consequent weakness.

Of the 72 patients with gallstone disease reviewed for this article, 63 had gallstones, and of these 4 died. The stones were distributed as follows: 44 times in the gall-bladder; 5 in the gall-bladder and cystic duct; 1 in the cystic duct alone; 3 in the gall-bladder and common duct; 1 in the gall-bladder and common and hepatic ducts; 1 in the cystic and common ducts; 4 in the common and hepatic ducts; and 4 in the common duct alone. For practical consideration we may divide the stone-bearing areas into two groups, placing in the first group all stones that were found between the fundus of the gall-bladder and the termination of the cystic duct; and, in the second, all stones found in the hepatic and common ducts. Of the 63 patients, 12 were males and 51 females. Most of the patients were between the ages of forty and sixty years. Nine patients had had enteric fever, but the typhoid bacillus was recovered from only 2, both of whom had experienced the disease within six months previous to operation. The typhoid bacillus was reported from cultures of 2 others, neither of whom had ever had enteric fever. The colon bacillus was found in 11, and *Staphylococcus aureus* in 3.

Of the 63 patients, the disease had existed one week or less in 8; one year or less in 21; from one to five years in 16; from six to ten years in 7; from eleven to twenty years in 6; from twenty-one to thirty years in 1; from thirty-one to forty years in 1; and the duration was not mentioned in 3. Chronic dyspepsia was the complaint of 32. The pain was sudden and sharp, or crampy or spasmodic, and located over the gall-bladder in 57, but dull and burning in 1. It was referred to the back in 6, to the right scapula in 28, and to both back and scapula in 9. There was tenderness over the gall-bladder in 44; over Robson's point in 9. Rigidity of the right rectus was present in 9 cases. Attacks came on at night in 16. Nausea was the complaint of 2; vomiting of 20; and both nausea and vomiting of 22. Chills were present in 10 cases; chills and fever in 4; chills, fever, and sweats in 14; chills and sweats in 1; and fever and sweats in 1. Jaundice was present alone in 27 cases; jaundice with clay-colored stools and biliruria in 10; while but 2 complained of itching of

the skin from jaundice; 15 patients had lost from ten to sixty-five pounds in weight; 4 patients found stones in the stools. The liver was enlarged in 16. The gall-bladder was determined enlarged clinically in 6. The stomach extended down near or to the navel in 5. Carcinoma of the liver was seen once.

Adhesions were found as follows: around the gall-bladder in 4; around the common duct in 4; gall-bladder and stomach, 10; gall-bladder and liver, 1; gall-bladder and colon, 2; omentum and gall-bladder, 8; omentum and liver, 3; omentum, stomach and colon to liver, 4; obliterating the foramen of Winslow, 1; omentum, stomach and colon to gall-bladder, 1; gall-bladder, liver and stomach, 1; omentum, colon and pylorus, 1; omentum, colon, pylorus and anterior parietal peritoneum, 1; liver and anterior parietal peritoneum, 1; omentum, colon and gall-bladder, 1; omentum, gall-bladder and duodenum, 1. A pericholecystic abscess was found once. The gall-bladder was small in 4 cases; thickened in 9; both small and thickened in 9; distended in 8; and both thickened and distended in 11. Hydrops was present in 4 cases; empyema in 3; and gangrene in 1. The gall-bladder was involved by acute cholecystitis in 1 case; by chronic in 7; by chronic with acute exacerbation in 20, of which 3 showed in addition necrosis, and 1 was hemorrhagic and oedematous. The common bile duct was thickened and dilated in 2 cases. In 2 instances the gall-bladder showed a diverticulum. The stones ranged in number from 1 to 213, and were variously described as yellow or black, round or oval, faceted or mulberry. Gravel was present in 1 case. The quantity of bile varied from a few c.c. to 50 c.c. and was clear or cloudy, reddish, greenish-yellow, or black, and viscid or inspissated. Enlarged lymph nodes around the cystic duct were palpated in 2 cases.

As regards the operative procedures, cholecystectomy was performed 30 times; cholecystostomy, 24; cholecystotomy, 1; and choledochostomy, 19. Drainage was freely used, a rubber tube being placed in the gall-bladder in 24 cases; in the cystic duct in 13; in the common duct in 13; and in the hepatic duct in 6. Supplementary dressings of gauze insulated by either a split rubber tube, or else by rubber-dam, reinforced the primary tubes in 36 cases, and were placed in the fossa of the gall-bladder in 25; in front of and behind the right edge of the lesser omentum in 16; and in the sub-hepatic region in 18. Examination of the blood revealed hemoglobin percentage between 50 and 70 in 19 cases; from 71 to 80 in 21; and from 81 to 96 in 22. Leukocytosis varied between 3400 and 10,000 in 36 cases; from 10,000 to 20,000 in 19; and from 20,000 to 40,000 in 3. The coagulation time of blood was five minutes or less in 34 cases; and from five to fourteen minutes in 19. In some few instances no blood report was received. Differential leukocyte counts, and examinations of stomach contents and of feces were made with few exceptions.

Interesting pathological features were met with as follows: A spontaneous cholecystogastrostomy, separation of which revealed an opening in the stomach the size of a goose quill, necessitating gastrorrhaphy. In another case the pancreas was slightly enlarged, and a few hard areas were palpated in it; from this patient 13 gallstones, the size of a pea, were removed from the common duct. In another patient, a woman, aged forty years, tissue hyperplasia around the fundus of the gall-bladder, invading the liver for from one-quarter to one-half inch, was seen at operation; the pathological findings revealed, in addition to chronic calculous cholecystitis with acute exacerbation, marked proliferation of the mucous membrane of the gall-bladder, enough to warrant a tentative diagnosis of adenoma. One intrahepatic gall-bladder was found, deeply embedded in the liver, firmly contracted upon contained stones, and shrunken, distorted, and thickened to such extent that certain landmarks were obliterated; a very large, square, faceted stone had partially ulcerated through the fundus of this buried gall-bladder. In 2 cases cholecystectomy was performed because of a distinct diverticulum in the gall-bladder of one, and of a diverticulum near the junction of the cystic with the hepatic duct in another. A gall-bladder that contained 213 stones had to be ablated because some stones were embedded in its mucosa. Another gall-bladder was removed because a stone that blocked the cystic duct could not be dislodged. In this case, several whitish, circumscribed, elevated areas, one inch square, and supposedly carcinomatous, were seen upon the visceral surface of the liver. In a case of cholecystostomy, in addition to a rubber tube with gauze being placed into the gall-bladder, this organ was attached to the anterior parietal peritoneum to meet the indication for prolonged drainage. In another case while cholecystostomy was performed, yet the rubber tube could not be invaginated into the cavity of the organ on account of the thickness of the gall-bladder mucosa.

A few of the many complications of gallstone disease are illustrated in this series. In 2 cases in which the stomach was dilated to a finger's breadth above the navel, there were found numerous adhesions between the gall-bladder and pylorus. Ulceration of the gall-bladder was seen in the case of spontaneous cholecystogastrostomy, and in the case of intrahepatic gall-bladder, in which a stone was caught worming its way through the gall-bladder wall. The adhesions and pericholecystic abscess, the empyema and gangrene of the gall-bladder, and adenomatous degeneration of its mucosa, the chronic pancreatitis and carcinoma of the liver have all been referred to. Empyema of the chest and pneumonia of the right lung were fatal complications in one case. In a patient who had been jaundiced during the ten days previous to operation, from chronic obstruction of the common duct, the liver extended almost to the navel, and was tender—conditions sufficiently accounted for

by finding 31 stones in the common duct, one of which was the size of a hickory nut, another in the ampulla, and 4 more in the left hepatic duct. Chronic appendicitis complicated one case of cholecystitis and 3 of cholelithiasis. I am not prepared to say in these 4 cases whether the appendix was primarily diseased and infected the gall-bladder secondarily through the portal system, or whether the infection extended from the gall-bladder to the appendix. In no instance was there impaction of a gallstone in the appendix, and this was certainly impossible in two of the appendices removed, since both were affected by chronic obliterative appendicitis. It is interesting to observe that a feature common to all 4 of these cases was prolonged indigestion, and this is noteworthy also because there were active simultaneously two of the most frequent causes of this malady, namely, chronic gallstone disease and chronic appendicitis.

Because of its frequency (about 15 to 20 per cent. in my cases), and because of the dire consequences when not removed, I shall say some few words on common duct lithiasis. In 29 out of 182 of my cases stones were found in the common duct and elsewhere, and merely to have removed the stones that were situated elsewhere, thereby overlooking those in the common duct, would have boded ill in any of the 29 cases. In the series of 63 cases of cholelithiasis now reported, stones were found in the common duct in 13. If these stones were not removed, nature might relieve the situation on behalf of the patient by the subsequent permanent external biliary fistula, mutely rebuking the surgeon for his bungling job, and patiently awaiting the aid of re-operation.

Although theoretically infection of the common duct directly from the intestine may be said to be resisted by the oblique intramural segment of the duct, and the presence of the terminal sphincter of Oddi, yet it is obviously impossible to say in how many people these supposed natural barriers have been prophylactic. It is true that the gall-bladder is infected by way of the common duct, though not so frequently as by the portal blood, and this organ is the primary focus for lithiasis of the common duct. While stones in the gall-bladder alone create much mischief, yet here the mischief is confined to a branch only of the biliary tract; but when stones pass out into the common duct and cannot pass through it the main line becomes blocked, and the entire biliary tract more or less involved. Stones in the common duct choke up more or less completely the total excrementitious filtrate of the whole liver, and as this filtrate contains whatever bacteria the portal blood could collect and the liver could not annihilate, the well-known severity of the symptoms of choledochus obstruction can thus readily be accounted for.

When acute this obstruction is complete, but the duct soon dilates from inflammation of its walls and *vis a tergo* of the bile, so that the obstruction becomes incomplete, or chronic, and the stone or stones are now at liberty to carry on the ball-valve action described by

Fenger. Perfectly in accord with the simple mechanical action is the behavior of the jaundice. At first rapidly reaching a deep color from acute complete obstruction, it slowly lifts as the duct dilates to allow partial drainage of the blocked bile, and it alternates at the will of the ball-valve stone. This ball-valve action is significant in several ways. In the first place, it is nature's method of dealing with an emergency by permitting drainage of the pent-up toxic fluids from the biliary vessels into the intestine. Then by variations in the jaundice it as much as tells the surgeon that the ailment is benign, for the jaundice of malignancy develops slowly and progressively and remains for all time. Finally, the ball valve helps to maintain Courvoisier's law by preventing enough backward pressure to dilate the gall-bladder.

Courvoisier's law is, of course, of no use clinically, but often affords a beacon light when the abdomen is entered. If there is chronic jaundice depending upon obstruction of the common duct, a shrunken gall-bladder is significant of calculous blockage of the choledochus, but a dilated gall-bladder indicates some other cause for the obstruction. This shrinkage of the gall-bladder is favored by the ball-valve action of the stone or stones as explained above, and is determined by inflammatory fixation of the contracted organ. Recently, M. R. Barker, of Chicago, has expressed the belief that Courvoisier's law is dependent upon the folds of Heister in the cystic duct: that in calculous obstruction of the common duct the normal action of these folds is not disturbed, thereby preventing dilatation of the gall-bladder by keeping the cystic duct closed; but in obstruction of the duct by pressure of a tumor, the diseased condition has involved either the folds of Heister or the nervous mechanism that controls them, or both, and their normal action is suspended or destroyed, allowing distention of the gall-bladder with bile and its own secretion.

In addition to the ague-like paroxysms of jaundice, colicky pain, and fever with the characteristic "steeple-chart" rises of Moynihan, subjects of choledochus obstruction are very apt to suffer loss in weight, a feature ascribed by Fenger, to "intermittent, frequent, ptomaine intoxication—that is, bile absorption—as well as to disturbed digestion" (Moynihan). So, too, associated pancreatitis is apt to be another factor. This loss of flesh must be borne in mind when questions of malignancy arise.

Illustrative of the above remarks is the following case: Mrs. S., aged fifty-nine years, had been a sufferer from gallstone disease for seven years, during which time she had had innumerable attacks similar to, but not as severe as, the present. Three months before operation she was afflicted with severe, colicky pain in the right hypochondrium, radiating to the back and right shoulder. The pain was followed by vomiting, and this by chills, fever, and sweats. Three weeks before operation the pain became very severe, the



attacks more frequent, and the jaundice very deep, with clay-colored stools. During the three weeks between this attack and the operation there was very little pain, and the jaundice began to clear, but the skin was very itchy. During these attacks the patient lost nearly 50 pounds in weight.

Examination showed universal jaundice and tenderness over the liver. Anemia to the extent of 68 per cent. of hemoglobin was present, and the blood coagulated within seven minutes.

Operation revealed in addition to adhesions between the omentum, pylorus, colon, and the gall-bladder, a small contracted and thickened gall-bladder free of stones. The common duct was much dilated, being as large as the little finger. A calculus the size of a marble was removed from the ampulla of Vater, and two smaller, irregular calculi from the hepatic duct. Drainage of the common duct was effected by a rubber tube, and of the sub-hepatic region and area in front of the lesser omentum, by Mikulicz drains.

By no means, however, will all cases be found so typical. In the absence of impaction no jaundice whatever may develop, and no severe pain arise. Endless modification of symptoms may be met with. Nevertheless, even in the absence of jaundice the common duct should always be determined free of stones.

In recent years pancreatitis has been recognized as a complication of gallstone disease. A small stone impacted in the ampulla of Vater may convert the bile and pancreatic duct into a single channel, thereby causing retrojection of bile and acute pancreatitis from irritation of the bile salts (chemical pancreatitis) and from the accompanying infection. Chronic pancreatitis may arise from extension of the inflammation from the common duct into the pancreas through the duct of Wirsung. Robson found pancreatic catarrh or interstitial pancreatitis in more than half his cases of common duct lithiasis. This is somewhat higher than the experience of W. J. Mayo who stated recently that in 268 operations on the common and hepatic ducts the pancreas showed disease in 18.6 per cent. I have found chronic pancreatitis in about 11 per cent. of my fatal cases of cholelithiasis. I report on these fatal cases, because in the living the diagnosis of chronic pancreatitis by palpation is very fallacious. As Richardson recently stated: "I would therefore exclude from all consideration of scientific accuracy my own cases, at least of so-called chronic pancreatitis, for their existence has never been proved by section, by microscope, or by autopsy. Palpation in these cases should always be directed first to the triangle of pancreatic inflammation, recently described by Mayo. This triangle is that part of the head of the pancreas which lies between the duodenum on the right of the ducts of Santorini above and Wirsung below. It is here that the organ is first infected."

If a stone in the common duct compresses the duct of Wirsung, the duct of Santorini will maintain pancreatic excretion in nearly

half of the cases (Mayo). Letulle and Nattan-Larrier found that in 10 per cent. of patients the common bile duct and the duct of Wirsung empty into the duodenum by separate orifices, and it might be supposed that in this way the pancreas would be exempt from involvement. This is true in so far as chemical pancreatitis is concerned, but inflammation could yet spread from the common duct into that of Wirsung by travelling along the small extent of duodenum between them, and this, perhaps, explains the pancreatic involvement cited in New's case (cited by Egdahl), in which gallstones were present, but the duct of Wirsung had a separate opening. In this connection it would be interesting to learn if the pancreas is ever infected from the duodenum through the duct of Santorini when this is present. Opie has well said that in this unfortunate association of terminal facilities the large percentage of known diseases of the pancreas have their etiology (cited by Mayo).

I have recently operated upon two cases of acute suppurative pancreatitis, both of which showed fat necrosis. Both cases were drained retroperitoneally, and both recovered. In only one, however, was associated gallstone disease found. Furthermore, pancreatic cysts also may arise from pressure of a gallstone upon the duct of Wirsung.

It is my routine practice in all cases of gall-bladder affections, in addition to examination of the blood and stomach contents, to have the feces examined. Fatty stools in the absence of jaundice are very significant of chronic pancreatitis. If the urine shows glucose, and if it yields the acicular crystals of Cammidge's test, the diagnosis of pancreatitis is strengthened. My experience with Cammidge's test has been limited to the latest two cases of suspected pancreatitis admitted in hospital. In the first case the test was positive; in the second, it was positive at the first trial, but negative at the second. Of these, one did not have the disease, and if the other patient had pancreatitis, no opportunity of proof by operation could be had.

The medical treatment of gallstone disease may be disposed of in a few words. The task of dissolving gallstones or absorbing adhesions by medical means may be conservatively estimated as about equal to the twelve labors of Hercules, or the recurring toil of Sisyphus. The Carlsbad treatment is very useful to hasten convalescence from gallstone operations, and is a good place for those who, in the absence of contra-indications, refuse to be operated upon, since it promotes mental peace.

I shall speak somewhat more fully on the surgical treatment. In my experience the cases to which the prophylactic treatment for gallstones could be applied were those referred to me early by physicians. In such cases the contents of the gall-bladder showed the formative elements of undeveloped gallstones, and the draining away of such material usually resulted in cure. After gallstones

have formed the risk of operation is the risk of delay, as I think I have shown throughout this paper.

My operative technique has recently been described<sup>4</sup> so that it is unnecessary to repeat it now. The principles that govern me in operations on the biliary passages are, in the first instance, those common to all abdominal operations, namely, to get in the abdomen as quickly as possible, to remain there as short a time as possible, and to get out as soon as possible, doing only that which seems necessary to restore the patient to health. I take pains in the proper disposal of packs, so as to wall off the operative field as completely as possible. Adhesions are avoided when they do not interfere with the proper execution of the operation. The biliary tract is searched for stones, and all that are encountered are removed. Free and sufficient drainage is instituted according to the requirements of each individual case. Postoperative treatment must be watchfully and intelligently supervised.

I do not favor cholecystotomy or choledochotomy without subsequent cholecystostomy or choledochostomy, and I believe that with the elimination of these two procedures the statistics of postoperative peritonitis would be considerably reduced.

Cholecystectomy is a procedure I avoid when possible. The gall-bladder should not be removed unless we feel that in its ablation we are taking away a menace to the future health and comfort of our patient. Sidney Phillips has well said that it is impossible for the surgeon to devise so perfect an automatic mechanism for storage and intermittent distribution of bile as the gall-bladder. Aside from the danger of hemorrhage attending cholecystectomy, we must look into the patient's postoperative future. If a second operation should at any time be required, we may be only too glad that we have previously preserved the gall-bladder as a valuable agent for drainage of the biliary tract, and that the operative field is comparatively free of adhesions, as is not likely to be the case if the gall-badder has been removed.

### ASCITES IN TYPHOID FEVER.<sup>1</sup>

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PERITONEAL effusion in typhoid fever, apart from peritonitis, must be of rare occurrence, as there is no reference to in it the literature on the subject. During the last three years six cases presenting

<sup>4</sup> Surg., Gynec., and Obstet., January, 1908, 61.

<sup>1</sup> Read at a meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1908.

signs of such effusion have come under my observation. In all of them the effusion occurred during the course of the illness, persisted for about ten days or two weeks, and disappeared in all but one with convalescence. In all the cases the illness was severe, but in none were there hemorrhages or symptoms of peritonitis, except in one case.

CASE I.—The most marked case was that of a woman, aged thirty years, who was married, had two children, and came from the foothills of the Rocky Mountains in October, 1907. On her arrival she was very ill, her temperature being 104° F. She had severe bronchitis, with loud rales of great variety and some wheezing in all parts of the chest. She had a history of asthmatic attacks extending over some years. The sputum was frothy and copious, but contained no spirils or eosinophiles, nor was the dyspnoea paroxysmal. After a few days it became evident that she was suffering from typhoid fever, all the usual symptoms of which were presented later—the rose-colored spots, enlarged spleen, leukopenia, Widal reaction, low blood pressure, etc. The abdomen was not at any time distended, but remained relaxed throughout. The course of the disease was severe and protracted, but otherwise uneventful. She showed marked prostration. In the third week after she was first seen both flanks became full and fluctuating in the dorsal position. The note to light percussion was flat to the mammillary line; on deeper percussion there was slight tympany of an amphoric character. Fluctuation was easily demonstrated. When turned on her side the upper flank became concave and somewhat tympanitic; the dependent one full and rounded with fluctuation and flatness well marked to the parasternal line. That these signs were not due to fluid feces in the colon was shown by the fact that no alteration in them resulted from the action of a copious enema. A purgative was then given; it acted freely but without affecting the signs of free fluid effusion. The quantity of fluid varied, diminishing somewhat on one or two occasions, and then increasing again, until toward the end when it gradually lessened and disappeared, leaving the flanks retracted. At the same time the temperature became normal, and convalescence was soon established.

CASE II.—A laborer, aged twenty-two years, with good personal and family histories, was admitted to the hospital September 22, 1905. He said he had had typhoid fever during the preceding year. However, the symptoms of the present attack were quite marked: the usual temperature, some diarrhoea, moderate abdominal distention, rash on the chest and abdomen, enlarged spleen, leukocytes as low as 4500, and well-marked Widal reaction. The illness was protracted, there being apparently a series of intercurrent relapses. The signs of fluid in the peritoneal cavity became apparent October 23, in the beginning of the fifth week, and were quite marked until December 6, after which they gradually abated, and

were not evident ten days later. The abdomen was quite relaxed throughout the illness, and was not tender on deep palpation. His convalescence was satisfactory, and he left the hospital in good condition. The sputum was scanty, but in such as there was obtained no tubercle bacilli were found on repeated examinations.

CASE III.—A man, aged thirty-five years, a clerk, was in the hospital at the same time as Case II. On admission the abdomen was tympanitic in all parts, including the flanks. The rash was profuse and widespread. Two days after admission the flanks were found full, flat on percussion to the mamillary line, and with fluctuation quite distinct. The signs of effusion lasted over three weeks and disappeared with convalescence. His recovery was satisfactory.

CASE IV.—A young man, entered the hospital in January, 1908; the symptoms of typhoid fever were well marked. About the end of the second week of illness signs of moderate peritoneal effusion developed, persisted for two weeks, and then disappeared rather rapidly. The ophthalmotuberculin test was made without any reaction following. After the temperature had been normal three days pleuritis of the left side began with much pain and moderate fever. The exudate was fairly free, although no fluid was obtained by the aspirating syringe. To determine whether it was due to tuberculous infection, a further test was made with old tuberculin subcutaneously. No reaction resulted.

CASE V.—The patient was a girl, aged fifteen years, whom I saw but once, in consultation with her physician, in the second or third week of her illness. There was a large quantity of fluid in the peritoneal cavity; the signs were first observed on the preceding day, although the effusion had probably been present for some time. The illness was severe, the temperature being over 104° F. There was no pain or tenderness in the abdomen; its walls were not rigid. Her physician informed me that signs of fluid disappeared a few days later, the patient making a good recovery.

CASE VI.—In this case the effusion was probably due to tuberculous peritonitis. A man, aged twenty-three years, was admitted to the hospital September 24, 1907, with a temperature of 101.8° F.; pulse, 80. He was employed washing in a garage and a fellow worker occupied the next bed, having taken ill at the same time. The symptoms of typhoid fever were well defined in both cases, and the disease ran a rather severe course. In the fourth week there occurred phlebitis of the left saphenous vein, with marked chills, the temperature rising to 108.4° F. after the first chill. A few days later there were signs of some exudate into, first, the left, and then the right pleura. Two weeks later, and seven weeks after admission, there were well-defined signs of peritoneal effusion, the quantity being greater than in any of the preceding cases. The abdominal wall was rather rigid and somewhat tender to firm pressure. The

temperature was slightly, but irregularly, elevated, and the leukocytes, which had been below 5000, rose to 12,000. A tuberculin test was made; there was no reaction to 0.5 milligram given subcutaneously, but 2 milligrams caused a well-marked reaction. Later, there was marked reaction to the ophthalmotuberculin test. His general condition improved, although the peritoneal exudate persisted. He left the hospital January 21, 1908, in good condition, but with a considerable quantity of fluid still in the abdominal cavity.

In at least four of these six cases the effusion, so far as can be determined, was due to pathological conditions resulting from typhoid infection. The immediate cause of the effusion is uncertain. The disease was severe and attended by much prostration. The abdomen was very relaxed and the contents therefore had little support, so that the vessels would easily dilate, permitting considerable stasis, or at least marked slowing of the current of blood, thus favoring serous exudation. It is possible, also, that the mesenteric glands were greatly enlarged, causing slight but sufficient irritation of the peritoneum to excite effusion.

Toxemia is another possible cause of the effusion. In hepatic cirrhosis something more than simple obstruction to the portal vessels is required to cause ascites. This may be a toxic substance which affects the hepatic cells so as further to obstruct the portal circulation, or alters the peritoneal epithelium so as to permit a more rapid escape of serous exudate and possibly also cause obstruction of the peritoneal lymphatic vessels, so that the exudate is less readily removed.

It is probable that in other diseases attended by prostration moderate effusion into the serous cavities may be more frequent than is suspected. Recently in a case of empyema with a bronchial fistula, there were signs of peritoneal effusion for some days during a period of marked prostration and moderate toxemia; they disappeared with the improvement in the general condition. Even in hepatic disease ascites may disappear rapidly, and that, too, without improvement in the patient's general condition. Such was the case in a woman who entered the hospital last winter with marked jaundice and ascites of recent onset. After a few days both the jaundice and ascites rapidly diminished and disappeared, although her general condition was growing worse. She gradually became comatose and died a few days later.

**LOBAR PNEUMONIA.****A STUDY OF 445 CASES, WITH SPECIAL REFERENCE TO THE  
DECREASED MORTALITY SINCE THE INSTITUTION OF  
THE FRESH-AIR TREATMENT.**

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THE following study is based on a consideration of 445 cases of croupous pneumonia admitted to the Philadelphia General Hospital between February 1, 1905, and December 23, 1907. The data were collected from the clinical histories, in a considerable number of which the facts had been verified by postmortem examination. All cases, which, by the latter method, proved to be instances of miliary tuberculosis, hypostatic pneumonia, etc., were excluded from this compilation. February 1, 1905, was chosen for the beginning of the present study, since this time marks the beginning of the fresh-air treatment, the pneumonia patients being isolated in a special ward in which the windows are constantly kept wide open regardless of weather or temperature. The statistics of males and females have been kept separately for the special reason that women with pneumonia, owing to lack of room and the relative fewness of their number, are still treated in the general medical wards in which only the ordinary hospital ventilation is employed, the windows being generally closed during the cold months of the year when most of the cases occur. Some years ago, before the institution of the fresh-air regime, a similar study of the pneumonia cases in the same hospital was made by Ashton and Landis,<sup>1</sup> based on a study of 991 cases. Since there has been no change in the character of the patients coming under observation or in the methods of treatment employed, except the constant and liberal supply of fresh air, it is interesting to compare the result of the two series of cases.

As was pointed out by Ashton and Landis, in considering pneumonia as it is seen at the Philadelphia General Hospital, we are not confronted with average, but with extreme and somewhat unusual types of this disease. The patients with whom we have to deal are, in the vast majority of instances, far advanced in years—inmates of the almshouse—who have come to await death within its portals. Nearly all of them are the subjects of advanced states of degeneration of their various viscera, among which high-grade arteriosclerosis and chronic nephritis are not the exception, but the rule. The foregoing statements apply with equal truth to the large number of

<sup>1</sup> AMER. JOUR. MED. SCI., June, 1905.

patients afflicted with insanity or chronic nerve disease who contribute to our large mortality. The second class of cases with whom we have to deal are, from a therapeutic standpoint, no less discouraging, namely, the large number of tramps and habitual drunkards who have reached the lowest depths of depravity and vice, who often wind up a prolonged debauch with an attack of pneumonia and are brought to the hospital with delirium tremens or in a moribund condition.

I was led to collect the present series of statistics by the fact that a considerable number of what appeared clinically to be hopeless cases recovered, and I wished to verify my impression. The mortality in Ashton and Landis' series was over 53 per cent. The general mortality in the present collection was 47 per cent., not a great difference it would seem at first sight; but when we eliminate the female cases we find that 170 among 383 males died, giving a mortality of 43.6 per cent., or 10 per cent. less than before the fresh-air treatment was adopted. If from this number we subtract those that died within twenty-four hours of admission—moribund when admitted—we get a mortality of 38 per cent. This, of course, is still considerably above the average of 25 per cent., which obtains throughout most of the hospitals the world over, but when we consider the class of cases with which we have to deal it is not so bad. Of the women on the other hand, of whom there were but 62 in the present series, 40 died—a death rate of 64.5 per cent.; excluding those who died within twenty-four hours of admission—2 in all—we still are confronted with a mortality of 61.3 per cent. This is extremely high even allowing for the fact that the mortality among women is generally greater than in men. This may be construed as evidence detracting from the beneficial effects of the fresh-air treatment, since in Ashton and Landis' series the male and female statistics were not separated, and their high mortality may have been largely the result of female deaths, the number of which was not stated. I am, however, of the belief that the decrease in mortality more than counterbalances the influence of the female deaths in the first series, a fact which is apparently substantiated when the total death-rate of the two series is compared (53 per cent. against 47 per cent.). Another element which tended to prevent a still greater reduction in mortality was the fact that a number of the male patients did not receive the fresh-air treatment during their whole stay in the hospital, since it is not the custom to transfer cases to the pneumonia ward until a positive diagnosis has been reached.

Aside from the constantly open windows and door there has been no innovation in the method of treatment employed. For the most part therapeutics has been symptomatic in character, mainly sedative or stimulating as the individual case seemed to demand. In other words, active delirium and insomnia were treated with bromides, opium, etc., asthenic cases with strychnine, caffeine, ammonia, digi-



talís, etc. It seems to me that in the average case perhaps too much stimulation has been employed. Owing to the erroneous conception of the pathology and therapeutics of pneumonia with which the average resident physician enters the hospital, it seems to be his almost invariable custom to prescribe strychnine from the beginning, to "keep up the strength" despite the fact that the patient's condition may be quite satisfactory without any stimulation whatever. The use of alcohol seems to be steadily falling more and more into disfavor, and justly so, since this drug does more to relax the vasomotors than to stimulate the heart; and it has been quite definitely shown by the experimental researches of Paessler and Rolly that the vasomotor system is the one which causes death in pneumococcic infection, and not the heart. It is not my purpose to take up the apparently endless question as to whether alcohol is or is not a food, but it does seem to me to have been shown by Bachman that alcohol possesses no power of sustaining action in an isolated rabbit's heart, such as does, for instance, grape sugar. On the other hand, it seems to be a fact based on prolonged clinical observation that habitual toppers, when attacked by pneumonia, are often benefited by reasonable amounts of this drug. Hay, who collected statistics of 150 pneumonia patients, found the mortality 15 per cent. lower among those who did not receive alcohol.<sup>2</sup> Eserine has been employed beneficially in a number of cases in which there was marked tympanites, an extremely serious symptom which generally bespeaks a high grade of toxemia, and exerts a very deleterious action on the circulation, respiration, and digestion.

Sponging with cold water has been used quite frequently and with good results, not so much for the purpose of reducing the temperature, which it does very satisfactorily, but more with a view to toning up the vasomotor system, for which purpose it seems to be our most useful remedy.

Digitalis is still used to an astonishingly large extent when one considers the impotency of this drug in febrile cases, a fact which has been repeatedly pointed out by careful observers, but which does not seem to be generally recognized. Personally, I have never been convinced that digitalis accomplished anything in cases having any considerable degree of fever. The inaction of digitalis in pneumonia was, I believe, first pointed out by Thomas,<sup>3</sup> in 1865. Inasmuch as digitalis acts on the heart chiefly through the vagus, it would seem that its failure in effect might result from paralysis of this nerve, since it has been shown by Schleske and Cyon that high temperatures in frogs do bring about such a paralysis; furthermore, Liebermeister's experiments in mammals indicated a similar state of affairs. Brunton,<sup>4</sup> however, who has especially studied this point,

<sup>2</sup> *Lancet*, 1904, 1, 1643

<sup>4</sup> *Circulation and Respiration*, 1906.

<sup>3</sup> *Arch. f. Heilk.*, 1865, p. 329.

found that "in the rabbit and probably other mammalian hearts, a temperature sufficiently high to produce stoppage of the heart, does not paralyze the vagus or the inhibitory apparatus through which it acts," although "it is possible that a longer exposure to a high temperature, such as occurs in fevers, may produce this result."

COMPLICATIONS. Among 445 cases (males and females being included) *acute pericarditis* was encountered 8 times, all of the cases being fatal. This incidence of pericarditis in 1.7 per cent. of the cases corresponds very closely to the general literature on the subject from which the following statistics were collected:

	Pneumonia.	Pericarditis.
A. H. Smith . . . . .	485	6
M. Huss . . . . .	2616	22
Townsend and Coolidge . . . . .	1000	3
Leudet . . . . .	83	6
Ormerod . . . . .	268	33
Flint . . . . .	133	8
Behier . . . . .	114	3
Dusoh . . . . .	369	3
Sturgis and Coupland . . . . .	161	3
Collective Invest Rep. . . . .	1056	2
Bischo . . . . .	11,442	62
Sturges . . . . .	16	6
Fisner . . . . .	460	13
Spence . . . . .	201	7
Hadden, McKensie, and Ord . . . . .	706	19
Schleinger . . . . .	173	4
Musser . . . . .	489	6
Norris . . . . .	509	4
Ashton and Landis . . . . .	991	1
McCrae, Fyshe, and Ainley . . . . .	486	16
Pye-Smith . . . . .	434	14
Sello . . . . .	750	7
Sears and Larrabee . . . . .	949	19
Meyer . . . . .	500	5
Juergensen . . . . .	5738	27
Grisolle . . . . .	58	3
Chatard . . . . .	665	31
Poehlmann . . . . .	239	5
Hay . . . . .	200	9
Anders . . . . .	275	14
Austin . . . . .	70	3
Petsold . . . . .	271	4
Kaller and Lefebvre . . . . .	109	1
Rychner . . . . .	616	17
Doubleday . . . . .	254	6
Meltzer . . . . .	4252	46
Bischo . . . . .	4231	20
West . . . . .	100	3
Satterthwaite . . . . .	55	5
Audeoud . . . . .	419	5
Jackson . . . . .	1320	22
Geo. W. Norris . . . . .	445	8
Total . . . . .	43,722	501
		(1.1%)

*Acute endocarditis* occurred 3 times. All of the cases terminated fatally. The collected literature on this subject is as follows:

	Pneumonia. Endocarditis.	
Aufrecht . . . . .	1501	1
Fisner . . . . .	230	2
Wells . . . . .	6050	19
Liebermeister . . . . .	204	1
Sello . . . . .	750	6
McCrae, Fyshe, and Ainley . . . . .	486	14
Musser . . . . .	489	1
Becker . . . . .	415	1
Meyer . . . . .	500	5
Norris . . . . .	500	5
Rychner . . . . .	616	8
Pye-Smith . . . . .	434	7
Juergensen . . . . .	5738	11
Dusch . . . . .	369	4
Petsold . . . . .	271	1
Hadden, McKensie, and Ord . . . . .	708	1
Collect. Invest Rep. . . . .	1065	1
Austin . . . . .	70	1
Hall . . . . .	70	1
Huss . . . . .	2616	4
Baeck . . . . .	340	1
Biaoh . . . . .	6885	15
Croce . . . . .	610	6
West . . . . .	100	0
Sears and Larrabee . . . . .	291	9
Chatard . . . . .	656	13
Omerod . . . . .	183	6
Audeoud . . . . .	419	4
J. M. Clarke . . . . .	126	1
Geo. W. Norris . . . . .	445	3
Total . . . . .	33,139	153 (0.46%)

*Empyema* occurred only twice in the present series. One case ended fatally, the other recovered. My collected statistics show the following incidence:

	Pneumonia.	Emphysema.
Chatard . . . . .	658	27
Middlesex Hospital . . . . .	287	9
Coll. Invest. Rep. . . . .	1085	5
Spence . . . . .	201	4
Gaitskell . . . . .	10	1
Townsend and Coolidge . . . . .	1000	6
Hadden, MacKenzie, and Ord . . . . .	708	6
Musser . . . . .	489	9
Norris . . . . .	500	6
Ashton and Landis . . . . .	991	3
Aufrecht . . . . .	1501	24
Meyer . . . . .	500	12
Sello . . . . .	750	24
Sears and Larrabee . . . . .	949	19
White and Pearce . . . . .	1341	45
Pye-Smith . . . . .	434	24
Futcher . . . . .	48	1
Hall . . . . .	70	5
Poehlmann . . . . .	239	7
A. H. Smith . . . . .	488	10
Kaler and Lefebvre . . . . .	100	1
Schlesinger . . . . .	173	7 children
McCrae, Fyche, and Ainley . . . . .	488	18
Doubleday . . . . .	252	15
Fisner . . . . .	230	4
West . . . . .	100	1
Audeoud . . . . .	419	22
Jackson . . . . .	1320	22
Morse . . . . .	118	9 children
Geo. W. Norris . . . . .	445	2
Total . . . . .	15,852	358 (2.2%)

*Pulmonary abscess* was encountered in two instances, one of them ending in death. My collected statistics are as follows:

	Pneumonia.	Pulmonary abscess.	
Huss . . . . .	2618	20	12 fatal
Sturges and Coupland . . . . .	267	1	
Grisolle . . . . .	280	1	
Bamberger . . . . .	186	1	
Morehead . . . . .	189	5	
Spence . . . . .	201	1	1 fatal
Flint . . . . .	133	4	2 fatal
Aufrecht . . . . .	1501	8	
Musser . . . . .	489	2	2 fatal
Steven . . . . .	120	2	2 fatal
Sello . . . . .	750	11	
Lebert . . . . .	898	4	
Sears and Larrabee . . . . .	949	3	
Baek . . . . .	340	1	
A. H. Smith . . . . .	304	1	1 recovered
Norris . . . . .	500	0	
Poehlmann . . . . .	239	1	1 fatal
Rychner . . . . .	616	0	
St. Barts Hospital . . . . .	1165	2	
Doubleday . . . . .	252	1	
West . . . . .	100	1	
Satterthwaite . . . . .	55	0	
Elsner . . . . .	150	11	
Fisner . . . . .	230	0	
Audeoud . . . . .	419	1	
Jackson . . . . .	1320	1	
Geo. W. Norris . . . . .	445	2	1 fatal
Total . . . . .	14,214	83	(0.5%)

No cases of *pulmonary gangrene* were recorded.

*Meningitis* was noted in 3 instances, with 2 deaths. In addition to these cases, there were 2 which presented marked symptoms indicating meningeal irritation, such as headache, vomiting, cervical rigidity or retraction, and delirium, but in which no actual palsies or ocular neuritis occurred. Both of these cases recovered. They were, therefore, classified as "meningismus," probably the result of toxemia. A diagnosis between the two foregoing conditions is often difficult, but, as a rule, may be settled by lumbar puncture. The collected statistics added to the present series give the following table:

	Pneumonia.	Meningitis.	Died.
Huss . . . . .	2616	2	2
Dusch . . . . .	630	7	
Coll. Ivnest. Rep. . . . .	1065	1	
Biach . . . . .	11,422	15	15
Chomel . . . . .	50	5	
Townsend and Coolidge . . . . .	1000	1	1
Norris . . . . .	500	4	1
Becker . . . . .	505	1	1
Flint . . . . .	133	1	1
Musser . . . . .	489	1	
McCrae, Fyabe and Ainley . . . . .	486	23	
Sears and Larrabee . . . . .	949	7	
Meyer . . . . .	500	5	
Chatard . . . . .	658	13	13
Aufrecht . . . . .	1501	4	
Nauwerk . . . . .	1172	14	
Sello . . . . .	750	5	
Juergenson . . . . .	5738	8	
Flamer . . . . .	230	6	
Fraenkel . . . . .	750	5	
Firket . . . . .	16,333	64	
Poehlmann . . . . .	239	1	1
Rychner . . . . .	616	7	
Mueller . . . . .	444	2	
Doubleday . . . . .	252	4	4
Audeoud . . . . .	419	12	12
Jackson . . . . .	1320	3	
Geo. W. Norris . . . . .	445	3	2
Total . . . . .	51,212	234	53
		(0.4%)	(Mortality 93%)

*Acute arthritis* as a complication occurred 3 times, twice ending in death. This is one of the rarer complications, which we find with increasing frequency in the later statistical study of pneumonia, for the reason that the joint involvement has in the past been attributed to an intercurrent rheumatism. It is, however, a true complication due to the local action of the pneumococcus. The condition has been so carefully studied and described by Cave, Herrick, and others, that a further consideration is at present unnecessary. In the literature the following cases have been reported:

	Pneumonia.	Arthritis.	Died.
Huss . . . . .	2616	22	2
Coll. Invest. Rep. . . . .	989	8	
Grisolle . . . . .	201	4	
Fox . . . . .	53	1	
Spence . . . . .	201	1	
Townsend and Coolidge . . . . .	1000	8	1
Hadden, MacKensie, and Ord . . . . .	708	40	13
Musser . . . . .	489	5	1
A. H. Smith . . . . .	488	0	
Sello . . . . .	750	1	
Ashton and Landis . . . . .	991	2	0
Norris . . . . .	500	1	1
Cave . . . . .	2292	2	
Sears and Larrabee . . . . .	949	23	7
Netter . . . . .	4156	6	
Ziemssen . . . . .	3293	2	
Fismer . . . . .	230	1	
Raw . . . . .	817	7	3
Petsold . . . . .	271	3	
Hall . . . . .	70	1	
Riesell . . . . .	445	2	
Rychner . . . . .	616	0	
Vogelius . . . . .	5158	6	
Hermann . . . . .	235	1	
Poehlmann . . . . .	239	0	
Sainter . . . . .	331	0	
Audeoud . . . . .	419	3	2
Croce . . . . .	610	1	
Jackson . . . . .	1320	1	
Clarke . . . . .	126	1	
Geo. W. Norris . . . . .	445	3	2
Total . . . . .	30,113	158	32

(0.5%) (Mortality 28%)

*Otitis media* occurred in 6 cases, 1 of which ended fatally. This is one of the complications which occurs more frequently in children than in adults, a fact which accounts for the paucity of these cases in the present series. It not infrequently produces symptoms which simulate meningitis, even when no actual meningeal involvement has occurred. A careful aural examination, in cases of pneumonia presenting atypical symptoms, is too frequently neglected. The collected statistics are as follows:

	Pneumonia.	Otitis.	Died.
Dusch (children) . . . . .	173	18	
Gross . . . . .	314	2	
Coll. Invest. Rep. . . . .	1065	2	
Norris . . . . .	500	2	0
Becker . . . . .	505	1	
McCrae, Fyshe, and Ainley . . . . .	486	19	
Sears and Larrabee . . . . .	949	16	
Pye Smith . . . . .	434	3	
Hall . . . . .	70	1	
Futcher . . . . .	48	1	
Morse (infants) . . . . .	118	21	
Musser . . . . .	489	4	2
Doubleday . . . . .	252	2	0
A. H. Smith . . . . .	488	6	0
Schlesinger (children) . . . . .	173	18	
Geo. W. Norris . . . . .	445	6	1
Total . . . . .	6508	122	3

(1.8%) (Mortality 1.5%)

*Parotitis*, another of the less common complications was recorded once, and this case terminated favorably. The infection of the gland in these cases may be either hematogenous or by way of Steno's duct. Comparing our incidence percentage with the general literature, we find:

	Pneumonia.	Parotitis.	Died.
Sturgis and Coupland . . . . .	123	1	
Mueller . . . . .	444	1	
Norris . . . . .	500	1	0
McCrae, Fyshe, and Ainley . . . . .	486	4	
Sears and Larrabee . . . . .	949	2	1
Musser . . . . .	489	1	0
Flint . . . . .	131	1	1
Geo. W. Norris . . . . .	445	1	0
Total . . . . .	3575	12	2
		(0.3%)	(Mortality 16%)

*Acute peritonitis* occurred only once in the present series, and ended in death. A good deal has been written on the subject of pneumococcic peritonitis lately, since primary peritonitis due to this cause is of no great rarity. Inasmuch as infection may take place through the genito-urinary tract, the condition is more common in females. Hematogenous and gastro-intestinal infection, according to Sulzer, also occur. In a good many of the cases there is a tendency for the inflammatory process to become encysted, and unless evacuated by incision, to rupture into the umbilicus, intestines, bladder, scrotum, etc. In cases secondary to pneumonia such events so far as I know have not been reported. Peritonitis complicating pneumonia has been reported as follows:

	Pneumonia.	Peritonitis.	
Fawcett . . . . .	182	5	
Mueller . . . . .	441	1	
Townsend and Coolidge . . . . .	1000	2	1 fatal
Musser . . . . .	489	1	1 "
Sears and Larrabee . . . . .	949	3	3 "
Norris . . . . .	500	1	1 "
Poehlmann . . . . .	239	1	1 "
Ryehner . . . . .	616	4	
A. H. Smith . . . . .	428	0	
McCrae, Fyshe, and Ainley . . . . .	486	3	
Hadden, McKensie, and Ord . . . . .	708	0	
Doubleday . . . . .	252	3	3 fatal
Chatard . . . . .	658	3	
Sello . . . . .	750	1	
Pye-Smith . . . . .	434	0	
Audeoud . . . . .	419	0	
Clarke . . . . .	126	2	
Geo. W. Norris . . . . .	445	1	1 fatal
Total . . . . .	9221	31	11
		(0.3%)	(Mortality 92%)

*Acute colitis* occurred in 4 cases; none of these recovered. *Phlebitis* was encountered once, the femoral left vein being involved,

with eventual recovery. The *urine* was examined for albumin in 397 cases; it was found in 311 (78 per cent.); 136 of these died (34 per cent.). Albumin was absent in 86 cases, of which 27 died (31 per cent.). There were records of 382 microscopic examinations. Casts were found in 236 cases, of which 106 died (27 per cent.). They were absent in 130 cases, of which 63 died (49 per cent.). Aside from these examinations a clinical diagnosis of acute nephritis was recorded 16 times, in 14 of which a fatal termination occurred (87 per cent.). It will be seen, therefore, that acute nephritis is one of the most serious complications of pneumonia. In the general literature the condition has been reported as follows:

	Pneumonia.	Acute nephritis.	Died.
Juergensen . . . . .	5738	66	
Huss . . . . .	2616	52	
Fizner . . . . .	230	1	
Zurich . . . . .	500	13	
Meyer . . . . .	500	3	
Norris . . . . .	500	3	
Becker . . . . .	505	2	
Nauwerk . . . . .	550	14	2
Musser . . . . .	489	6	4
Sello . . . . .	750	6	
Aufrecht . . . . .	1501	16	
Rosenstein . . . . .	130	2	
Wagner . . . . .	150	4	
Fraenkel and Reiche . . . . .	956	6	4
Ashton and Landis . . . . .	991	5	3
Mayer . . . . .	44	2	
Petsold . . . . .	271	7	
Hadden, McKennie, and Ord . . . . .	708	3	1
Townsend and Coolidge . . . . .	1000	9	4
Dusch . . . . .	369	3	
Sturgis and Coupland . . . . .	91	14	
Spence . . . . .	201	8	4
Flint . . . . .	133	2	
Audeoud . . . . .	419	6	6
Clarke . . . . .	126	1	
Poehlmann . . . . .	157	1	
Morhart . . . . .	139	2	
Baech . . . . .	340	6	
Geo. W. Norris . . . . .	445	16	14
Total . . . . .	20,107	268	42
		(0.5%)	(Mortality 57%)

The following list shows the diseases in which pneumonia appeared as an intercurrent infection, frequently a terminal one. The gravity of the affections is such as to require no comment on the high mortality which resulted:



	Total.	Died.	Mortality. Per cent.
Chronic nephritis . . . . .	45	41	93
Delirium tremens . . . . .	24	18	64
Arteriosclerosis <sup>a</sup> . . . . .	36	36	100
Myocarditis . . . . .	22	21	95
Alcoholism <sup>b</sup> (in addition to the above) . . . . .	62	37	59
Uremia . . . . .	5	5	100
Chronic endocarditis . . . . .	5	5	100
Mitral . . . . .	10	8	80
Aortic . . . . .	4	2	50
Erysipelas . . . . .	7	6	85
Pulmonary tuberculosis . . . . .	16	9	56
Hepatic cirrhosis . . . . .	2	2	100
Insanity . . . . .	4	3	75
Syphilis <sup>c</sup> . . . . .	10	5	50
Morphinism . . . . .	1	1	100
Hemiplegia . . . . .	1	...	...
Measles . . . . .	3	3	100
Pertussis . . . . .	2	2	100
Typhoid fever . . . . .	3	3	100

The extremely high mortality, which is shown in the foregoing table in the chronic nephritis cases, is due to the fact that only the severe types of this disease were recorded in the clinical diagnosis as such. As has been previously pointed out, albumin was found in the urine in 78 per cent. of the cases, and casts in 53 per cent.

The *sputum* was examined in 156 cases, with the following results:

	Times.
Pneumococcus present . . . . .	139
Pneumococcus absent . . . . .	10
Streptococcus present . . . . .	4
Staphylococcus present . . . . .	2
Micrococcus catarrhalis present . . . . .	2
Streptothrix . . . . .	2

Blood cultures were made in 16 cases; and the following organisms were found:

	Times.
Pneumococcus present . . . . .	8
Staphylococcus present . . . . .	2
Negative results . . . . .	4

Four patients in whom pneumococci were cultured from the blood recovered, 2 died. Of the 4 cases in which blood cultures were sterile 3 died and 1 recovered. One pure staphylococcus case recovered. One in which the last-named organism and the pneumococcus were found together died. It will be seen, therefore, that no prognostic conclusions can be drawn from the presence of pneumococci in the blood. The frequency with which they are recovered is largely

<sup>a</sup> The frequency of this condition is certainly underestimated. In many histories the condition was unrecorded except when very striking objective appearances were present.

<sup>b</sup> The proportion of intemperate subjects is also underestimated in the histories. Only those cases were collected in our statistics which were put down as habitual drunkards or in words to that effect.

a question of technique. It is probable that in every case pneumococci gain entrance to the blood stream. Cases have been reported in which this organism has been recovered from the blood when there was no evidence of pneumonia or any other grave systemic disease. The recent experiments of Tizzoni and Panichi<sup>7</sup> have shown that the pneumococcus may remain in the blood of animals for months after inoculation regardless of whether or not an active or passive, a partial or a complete, immunity had been developed previous to the inoculation. They have suggested, therefore, that recurrence of attacks of pneumonia are due to the fact that the organism has never been eliminated from the blood, and that some temporary lowering of resistive power has enabled them to gain a fresh foothold and renewed virulence. These authors also found that in some animals infection was unattended by symptoms of illness, but that if a trauma was inflicted, localized infection occurred at the point of injury, and sometimes ended fatally. In the present series there were 2 cases which followed close upon injury to the chest. One of these cases died, one recovered.

Pneumococcemia, or the presence of this organism in the oral or respiratory passages of apparently healthy people, explains how a temporary reduction of individual resistance may precipitate an attack of pneumonia. It has been shown experimentally, by Lode and Lipari, that the old idea about chilling of the body as a predisposing factor of pneumonia rests on a solid basis. The first-named author found that animals shaved to the extent of one-half or one-third of their integument, if exposed first to heat, then to cold, and finally inoculated with pneumococci, developed pneumonia and pleuritis much more frequently than did the controls, the ratio being as 85 to 12.

*Leukocyte counts* were made in 189 cases. When more than one count was made the highest was taken for our statistics:

	Cases.	Died.	Mortality. Per. cent.
Below 10,000 leukocytes . . . . .	27	11	40
Between 10,000 and 20,000 leukocytes . . . . .	81	25	32
Between 20,000 and 30,000 leukocytes . . . . .	55	14	25
Between 30,000 and 40,000 leukocytes . . . . .	17	6	35
Between 40,000 and 50,000 leukocytes . . . . .	6	3	50
Between 50,000 and 60,000 leukocytes . . . . .	2	0	0

These figures illustrate what is, I believe, generally accepted regarding the prognostic significance of leukocytes, namely, a count ranging between 10,000 and 30,000 is most favorable. Higher figures often indicate suppurative complications and are, therefore, to be regarded with suspicion; whereas, leukopenia bespeaks lack of reaction and is, therefore, to be unfavorably interpreted. The highest count met with in the present series was 57,000 and occurred

<sup>7</sup> Centralbl. f. Bakt., 1905, xxxvi, 25.

in a case complicated by phlebitis, which subsequently developed an abscess of the lung, but eventually recovered. Of late a renewed interest has attached itself to the question of leukocytes in relation to the opsonic index. The subject has been studied by MacDonald<sup>9</sup> Wolf,<sup>9</sup> Potter, and Krumwiede,<sup>10</sup> and quite uniform results have been reported. During the early stages of pneumonia there is a subnormal opsonic index, which in favorable cases increases gradually, and at the time of the crisis rises considerably above the normal. Wolf found that as the opsonic index increased the actual number of leukocytes diminished, making it appear that in the early stages the increased number of white corpuscles counteracted the deficiency of the opsonic power, a fact which has apparently been substantiated by Rosenow's<sup>11</sup> investigations. The opsonic index was examined in only one case of the present series, in which it was reported as being 2.15 on the day of the crisis. Rosenow found that an inverse relation existed between the number of leukocytes and the number of pneumococci in the blood.

Among the somewhat unusual and interesting results tabulated, the following may be mentioned:

Three patients passed intestinal parasites while in the active stage of pneumonia; 2 of these died. Attention has long been called to the fact that such an event occurs.

Nine of the patients were in their second attack; of these 6 died, a somewhat unusual occurrence, since second attacks are often milder than primary ones; 4 of the patients were attacked for the third time; 3 of these recovered. I have no doubt that these figures underestimate the frequency of repeated attacks. The question is often not put by the resident physician who takes the history, and in very many of the cases, owing to the patient's inability to speak English, or to the fact that they were admitted in a delirious condition no history was obtainable.

Delayed resolution occurred 6 times. All of these patients eventually recovering at least to the extent of being able to leave the hospital. Relapses occurred in 4 cases; 2 of these died.

So-called ether or operative pneumonia occurred in 3 instances, 1 of these terminating in death. The etiology of this condition is somewhat obscure. There are a number of predisposing factors which come into play: (1) It has been shown by Snel that ether reduces the bactericidal power of the lungs; (2) chilling of the body which occurs as the result of a loss of heat from the skin and the respiratory passages may play a part; (3) some cases are purely coincident and would have been disclosed if the lungs had been carefully examined before the operation; (4) pneumonia occurs after operations in which no ether is used, even when

<sup>9</sup> *Trans. Path. Soc., London*, 1906, lvii, 45.

<sup>9</sup> *Jour. Infect. Dis.*, 1906, iii, 731.

<sup>11</sup> *Jour. Amer. Med. Assoc.*, 1905, 871.

<sup>10</sup> *Ibid.*, November, 1907.

done under local anesthesia, especially after abdominal sections, and apparently result from emboli; (5) we have to consider the possibility of the aspiration of infectious material into the alveoli of the lungs.

Operative pneumonia has been reported with the following frequency:

	Operation.	Pneumonia.	Mortality.
Anders . . . . .	57,842	46	
Hewitt . . . . .	2910	3	
Rumboll . . . . .	1500	6	
Gurit . . . . .	52,177	30	
Derjuskinsky . . . . .	4946	43	0.4%
Kuemmell . . . . .	1017	40	28
Henle . . . . .	1787	143	65
Bibergall . . . . .	3009	135	
Schultze . . . . .	5724	27	
Kelly . . . . .	1800	8	
Rothrock . . . . .	489	5	3
Silk . . . . .	5000	13	
Gebels . . . . .	1196	77	53
Total . . . . .	140,397	570	(0.4%) (Mortality 45%)

Anyone, I think, who has the courage to try the fresh-air treatment, and sufficient persuasive power over the patient's relatives to allow it to be tried, will, I am convinced, never abandon it, even though the future may bring us a specific for pneumonia in the form of a curative serum. Of course, it takes time to eradicate prejudices and to change beliefs. It has not been so very long since patients with tuberculosis were advised to spend their time in closed rooms before a stove. It is an even shorter time since pneumonia patients were swathed in poultices, enveloped in jackets, and kept in rooms in which even the windows and doors were made as air-exclusive as possible by stuffing cotton into the cracks. We have gradually dispelled the fear of cold sponging and bathing in typhoid fever, and we will in time abate the dread of fresh air in pneumonia.

I shall never forget a big negro, in the third day of his pneumonia, whom I saw in the general medical ward, restless, fevered, and panting, the typical picture of the anguish which one so often sees in these cases. An hour later I saw him in the pneumonia ward whither he had been promptly transferred. It was a cold day in March, the windows and the door were wide open, so that there was a constant current of fresh cold air blowing over the beds. The patient greeted me with a smile, displaying a fine line of teeth which contrasted strikingly with his Ethiopian blackness, and remarked, "Fo de Lawd, Doc, I feels lak anoder man down hyar." This is not an isolated or exceptional incident, numbers of patients desperately ill have told me, upon inquiry, that they felt "pretty good." If then we can show not only an increased *bien faire* on the part of the patient, but also a reduced mortality, and an absence of deleterious effects why should not this method of treatment be the usual instead of the exceptional one?

THE PHARMACOLOGY OF HEART STIMULANTS.<sup>1</sup>

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A SUBJECT so broad as that covered by the title of this paper cannot be considered within a reasonable limit of time, and I shall therefore confine my remarks to those drugs which are classed together as the digitalis group, and to those pharmacological points which are of interest especially to the medical therapist. In discussing this subject I shall consider first one or two noteworthy facts common to the whole group, and, then, the points of individual difference of its more important members.

There are three essential factors in the action of these drugs which interest clinicians: (1) The stimulant influence upon the cardio-inhibitory mechanism which prolongs the diastole and thus slows the pulse; (2) the increase in the tonicity of the heart muscle leading to a more complete and more powerful systole; and (3) the constriction of the bloodvessels. The dicrotism, the incomplete diastole, and the incoordination of the heart, which are produced by very large doses of digitalis, are toxic manifestations and of minor importance to the therapist.

The action of digitalis in slowing the pulse is, I believe, a much more important factor in its beneficial influence in heart disease than is generally deemed. It is evident that if the quantity of blood thrown out by the heart at each contraction were constant, then the more slowly the heart beat the less blood would be pumped in a given time; in other words, if the volume of the pulse remained the same the rate of the pulse would be an accurate criterion of the work performed, and an inhibitory stimulation would mean less work done by the heart and consequent reduction in the blood pressure. But the volume of blood expelled at each contraction does not remain the same. The longer the diastole, within reasonable limits, the larger is the volume of the pulse wave. It has been shown experimentally by Elving and Wendt<sup>2</sup> and others that there is a degree of compensatory correlation between the rate and the volume of the pulse so that the amount of blood pumped by the heart per minute tends to remain constant despite variations in its rate.

The mechanism of this arrangement is not difficult to apprehend if we remember that the slowing of the pulse depends chiefly upon the prolongation of diastole. The lengthening of the period of auricular relaxation allows more blood to flow from the great veins

<sup>1</sup> Read at the meeting of the American Therapeutic Society, Philadelphia, May 7, 1908,<sup>2</sup> Skand. Arch. f. Physiol., 1907, xix, p. 96.

into the auricle, either of the right or left heart as the case may be; and the prolongation of the ventricular diastole permits the auricle completely to empty its contents into the ventricle, so that when that chamber begins to contract it finds itself well filled with blood, and consequently the pulse volume is increased. Although according to the experiments quoted the increased volume is ordinarily not sufficient entirely to compensate for the diminution in the pulse rate which results from stimulation of cardiac inhibition and the amount of blood per minute pumped may be somewhat lessened, nevertheless, it seems to me that the heart beating at a slow rate is working more economically than the rapidly acting organ.

If the ventricle begins to contract at a time when it is only half filled with blood, half of the effort of contracting is wasted in reducing the size of the chamber to correspond to the small amount of blood which is within it. On the other hand, if the ventricle is completely filled with blood before it begins to contract it is evident that all of the shortening of the cardiac muscle fiber which takes place does useful work; therefore the bigger the pulse volume the more work does the heart accomplish with the same expense to its total power, and consequently the more slowly the heart acts the more sparing is it of its reserve energy, and it obtains as well a longer period for rest and reconstruction.

In cases of chronic heart disease, when it is essential to make the burden thrown upon the feeble heart as light as possible, it appears to me highly important that we do what we can to slow the pulse, and the inhibitory stimulation of digitalis becomes *the* beneficial factor in its effects. The mere stimulation of the heart muscle is a matter of minor importance. What necessity is there for, or advantage derived from, the elevation of blood pressure? Dyspnoea, local congestion, or œdema may be temporarily relieved by other heart stimulants, as caffeine or ammonia; but is the patient any farther from the grave because some local evidence of heart weakness is concealed?

The objection has been raised against this view, that inhibitory stimulation tends to a relaxation of the muscle which might encourage a further dilatation of a weak cardiac wall, but here the action of digitalis in increasing the tonicity of the heart muscle comes into prominence as a preventive of this danger.

The only one phase of the effect of digitalis in increasing the muscular vigor of the heart, which I think needs emphasis at this time, is that in no other portion of the heart is the influence of the drug felt in the same way as it is in the left ventricle. Although the observation of Kaufmann that the diastolic, as well as the systolic, pressure in the left ventricle is augmented by digitalis indicates that the force of the auricular systole is to an extent increased by digitalis, yet it is a common occurrence to see the ventricle of the frog's heart firmly contracted in systolic spasm, while the dilated

engorged auricles are making ineffectual efforts to force blood into the larger cavity.

This fact becomes of importance in certain cases of mitral regurgitation when the ventricular muscle has undergone a larger degree of hypertrophy than has the auricle. Under the influence of digitalis the ventricle may drive the blood backward through the leaky mitral valve so vigorously as to overcome the muscular resistance of the feeble auricle and lead to further dilatation of that part of the heart. Moreover, in these cases the second defense, the right ventricle, will likely prove insufficient, for the experiments of Bayet<sup>3</sup> as well as my own studies<sup>4</sup> have shown that the action of the drug upon the right heart is comparatively insignificant.

There remains of the physiological actions of digitalis to be considered, its vasoconstricting influence. This action has frequently been regarded as a harmful by-effect to be avoided or combated, a point of view which I believe has at times led practitioners to adopt irrational or even injurious measures.

It is of course true that it requires more force to drive the blood through narrow arteries than it does through dilated ones, but it is equally true that in many cases the vascular contraction is a conservative effort on the part of nature to maintain the circulatory equilibrium. The coronary arteries are comparatively small vessels springing at right angles from a large trunk, a condition which is in many ways unfavorable for the entrance of blood into them. It is evident, therefore, that a considerable degree of pressure in the aorta is an absolute requisite for good coronary circulation. Tigerstedt and Johansson<sup>5</sup> have shown that in states of very low arterial tension despite the diminished resistance in front of it the ventricle may be unable to empty itself as completely as normally, a phenomenon most rationally attributed to lessened heart power the result of insufficient nutrition.

I do not mean to infer that the vascular effects of these remedies is never detrimental. There is scarcely room for doubt that when, as a result of degenerative changes in the muscle or an extreme degree of dilatation, the muscular tissue of the ventricle is too scanty to respond properly to the tonic influence of digitalis, the increased resistance to the flow of blood may work great damage. But I do think that these cases are much less frequent than is generally believed. Clinicians should not be too hasty in their efforts to dilate the vessels in cases of chronic heart disease; especially so since almost the only agents which we possess for this purpose, the nitrites, are substances which increase the rate of the pulse and must therefore tend to counteract the beneficial influence of digitalis in slowing the heart. The only reason that more harm has not been accomplished by the

<sup>3</sup> Acad. Royale de Med. Belg., 1892.

<sup>4</sup> Amer. Jour. Physiology, 1902, vi, p. 283.

<sup>5</sup> Skand. Arch. f. Physiol., 1891, ii, p. 409.

use of nitroglycerin in heart disease is because the method in which it is habitually given precludes any possibility of its having serious influence upon the circulation. The effects of a single dose of nitroglycerin last on an average about three-quarters of an hour, or, perhaps, under favorable conditions, an hour. How great is the folly, therefore, to administer it three times in the twenty-four hours and expect any permanent result.

I now come to the consideration of the differences in the effects of the individual members of this group of remedies. The digitalis drugs which are used practically are digitalis, strophanthus, squills, apocynum, and adonidin.

Squills and apocynum, on account of their irritant action upon the gastro-intestinal tract and upon the kidneys, are of practical utility only in selected cases, so that I shall dismiss them without further consideration.

There is a widespread belief that strophanthus differs essentially from digitalis in that it exercises little or no influence upon the bloodvessels; a belief for whose truth I have sought in vain for any convincing scientific evidence. This much, at least, has been clearly demonstrated by the work of Gottlieb and Magnus<sup>6</sup> and more recently by Tigerstedt,<sup>7</sup> that the action of strophanthus upon the vessels is a very marked one and even if it be a less powerful influence than that of digitalis, the difference is comparatively slight. There is, however, one important distinction between the action of these drugs, namely, that strophanthus is less likely to give rise to cumulative toxic symptoms than is digitalis, a fact of general clinical experience which has been experimentally confirmed by Fraenkel.<sup>8</sup>

Of adonidin our knowledge is far from satisfactory. It seems well established that its effect on the heart muscle and on cardiac inhibition are similar in kind, if somewhat less powerful in degree, than those of digitalis. On the other hand, Kakowski<sup>9</sup> found that whereas strophanthus and digitalis both constricted the coronary arteries adonidin widened them, a suggestive observation the precise bearing of which in our present state of ignorance is not clear. It is a remedy of promise, but, although it has now been before the profession for nearly thirty years, it remains still in the stage of promise.

In cases of chronic heart weakness, when merely the cardiac action of this group is desired, digitalis itself yet stands supreme. I wish, however, to say a few words concerning the search for the active principle of this drug, or for a substance which would represent its therapeutic virtues in small bulk. Moved by a desire partly for scientific accuracy in dosage, partly for a convenient form

<sup>6</sup> Arch. f. Exper. Path. u. Pharm., 1901, xlvii, p. 135.

<sup>7</sup> Skand. Arch. f. Physiol., 1907, xx, p. 115.

<sup>8</sup> Arch. f. Exper. Path. u. Pharm., li, p. 84.

<sup>9</sup> Arch. Internat. de Pharmacodyn. et Therap. xv, p. 21.



of administration, and partly by the love of the novel, clinicians have from time to time experimented on their patients with various of the glucosides which have been found in the digitalis leaves. At present digitoxin holds the foreground among these substances; but this much is clear, that if there be any single principle which represents completely the therapeutic virtues of digitalis that principle is *not* digitoxin. In the first place Fraenkel has shown that of all the digitalis glucosides digitoxin is the most dangerous and the most cumulative in its action; secondly, the work of Gottlieb and Magnus would indicate that digitoxin is decidedly more active in its vasomotor effects than either digitalis itself or strophanthus; and, thirdly, Kakowski experimenting with digitalin, digitalein, and digitoxin, was able with none of them to produce the increase in the contracting power of the heart that is brought about by digitalis.

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### ATAXIA OF THE HEART MUSCLE.

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SINCE the simultaneous graphic registration of venous and arterial pulses has been generally adopted, following the pioneer work of Mackenzie,<sup>1</sup> we have learned that dissociations in the activity of the different heart chambers occur very much more frequently than we formerly supposed. The dissociation of auricular and ventricular contractions has been generally accepted since the publications of His, Mackenzie, and many other writers. The anatomical cause has been shown to consist in a lesion of the bundle of His, reproduced experimentally by Hering<sup>2</sup> and Erlanger<sup>3</sup> and shown pathologically by Stengel,<sup>4</sup> and Ophuls and myself.<sup>5</sup>

Only lately the discussion of the possibility of hemisystole, an isolated contraction of one side of the heart, while the other remained in diastole, has been taken up.

Twenty years ago von Leyden<sup>6</sup> reported several cases in which he tried to explain by a hemisystole the phenomena observed in cases of mitral disease. In those cases two apex beats and two pulsations of the jugular vein corresponded to one arterial pulse; the first apex beat with a corresponding arterial and venous wave was supposed to correspond to a complete contraction of both heart chambers; while the second apex beat with a venous wave, but without an

<sup>1</sup> Study of the Pulse.

<sup>2</sup> Jour. of Exper. Med., 1906.

<sup>3</sup> Deut. Arch. f. klin. Med., vol. lxxxvii.

<sup>4</sup> Pfüger's Archiv., 1906, cviii.

<sup>5</sup> AMER. JOUR. MED. SCI., 1906.

<sup>6</sup> Ztschr. f. klin. Med., vol. lxiiv.

arterial pulse, was thought to correspond to an isolated contraction of the right ventricle.

This view advocated by von Leyden and defended again recently, has not been generally accepted. Riegel especially tried to show that the phenomena could be more easily explained by the theory that the second beat corresponded to a premature contraction of the whole heart, and that the absence of the arterial pulse could be explained by the fact that the left ventricle during the short diastole had not recovered sufficient strength to overcome the arterial pressure and open the aortic valve. This view has been generally adopted, and by the work of Wenckebach, Hering, Cushny, and Mackenzie has been shown to be the cause of the supposed hemisystole in the great majority of cases.

The possibility of a hemisystole has been denied on physiological and anatomical grounds, especially by Hering who admitted the occurrence of hemisystole only as a symptom of agony in a dying heart. Notwithstanding the authority of such an excellent observer as Hering, the occurrence of hemisystole has been very widely discussed in recent years.

It was again Mackenzie who first published some tracings in which there was an incongruence in the number of apex beats, indicating the action of the left ventricle, and the number of venous pulsations. He considered these tracings as very exceptional, and admitted the incongruence of the left and right heart action to be a symptom of beginning death.

The question of hemisystole was taken up again by F. Kraus and G. Nicolai,<sup>†</sup> who published a preliminary communication on this question. They studied the question by the graphic method in the perfused heart and by the electrodiagram in the human heart, and reached the following conclusions: If ventricular extrasystole is produced by direct stimulation, the ventricle in which the extra stimulus is produced contracts more strongly than the ventricle to which the stimulus has to be transmitted. If one diminishes the intensity of the stimulus, the contraction of the second ventricle becomes weaker, until a point is reached at which the first ventricle contracts, while the second one does not register any change in the intraventricular pressure. Such conditions arise in the human heart, if the extrasystole proceeds from the left ventricle. Here all the variations may be observed, deviation in the strength of the contraction and deviation from the synchronism of the contraction, until complete hemisystole occurs.

A second method by which the occurrence of hemisystole could be shown consisted in the electrocardiogram taken by Einthoven's method. Krause and Nicolai assert that the electrocardiograms of the left and the right ventricle are different from each other and

<sup>†</sup> Deut. med. Woch., 1908, p. 1.

are characteristic of the contraction of either left or right heart. The electrocardiogram taken over the heart during a ventricular extrasystole shows by variations in its form the part which the left and the right ventricle are playing. The form of the electrocardiogram also indicates the point from which the extrasystole starts, whether from the left or from the right ventricle. In some cases the electrocardiogram assumes the form of a purely right-sided cardiogram; under those conditions a hemisystole of the right ventricle may be diagnosticated.

The views expressed by Krause and Nicolai and the arguments for their validity cannot be judged at the present date, as the experimental evidence for their conclusions is not fully published, and as the value of the electrocardiogram, its interpretation, and especially the differentiation of the left and the right ventricular curves are not fully established and accepted.

Recently Wenckebach<sup>4</sup> has reported a case in which he was able to show the existence of dissociation in the activity of the ventricles. He drew attention to the fact that in cases of perpetual arrhythmia the disappearance of murmurs in extrasystoles points to the fact that not the whole ventricle is contracting, but only certain parts of it. The same conclusion can be reached by the fact that the height of the pulse does not depend upon the length of the preceding diastole, as under normal conditions. In several tracings of the apex beat obtained in a case of perpetual arrhythmia a superposition of three systoles could be demonstrated, each following systole beginning before the preceding had ended. As during systole the heart muscle is refractory to any stimulus, the conclusion had to be reached that the second systole began in a part of the heart muscle which had not contracted during the preceding systole. The case, therefore, proves the existence of partial contractions of the ventricle. Similar dissociations in the activity of the two auricles and the venous sinus were reported in the same exceedingly interesting paper of Wenckebach.

According to modern literature, therefore, we must distinguish between two varieties of dissociation of the activity of the ventricles: (1) Hemisystole consisting of alternating contractions of the left and the right chambers of the heart; and (2) partial contractions of the heart muscle, for which I propose the name of "ataxia of the heart."

Dissociation of the activity of the ventricles seems to be very rare, as very few convincing observations of this condition have been published. I have encountered it only once amongst a very great number of tracings obtained from heart cases. As the condition may be of some interest I shall briefly describe the phenomena observed in the patient:

<sup>4</sup> Archiv f. Anat. and Phys., Phys. Abteil.

E. B., aged twenty-seven years, Italian, entered the hospital on November 29, 1907, complaining of swelling of the legs, shortness of breath, cough, and pain over his heart. He had rheumatism about seven years ago in his right knee, incapacitating him for about three or four days, but otherwise he has never been ill. In April, 1907, he had a first attack of insufficiency of the heart with shortness of breath and cough lasting for about two months; lately these symptoms have returned, aggravated by marked sleeplessness and pain of an anginoid character. In the last few weeks he has noticed swelling of the legs.

On admission the patient presented the picture characteristic of combined failure of the left and right ventricles. His skin was extremely pale and seemingly exsanguinated, spotted at the ear, cheeks, and lips by deeply cyanotic areas; there was quite an appreciable amount of oedema extending to the knees. The respiration was quite labored, varying between 30 and 40 per minute. The pulse was very irregular in force and rhythm; comparing it with the apex beat one could easily notice that a large number of heart beats did not reach the wrist. The veins of the neck were markedly distended and pulsated. The apex beat could be felt, very heaving in character, in the seventh interspace in the anterior axillary line; the right heart border was 2 cm. to the right of the right sternal border, the upper border at the third rib. Over the whole area of the heart a systolic thrill could be felt. On auscultation such a multiplicity of murmurs were heard, that it was at first impossible to come to a clear conception of the valvular lesions. After the heart had slowed down under the influence of digitalis, a long drawn-out systolic murmur was audible at the apex, preceded by the sharply clicking sound of mitral stenosis. The second sound was very indistinct, and was followed by a long drawn-out diastolic murmur extending to the beginning of next systole. Over the tricuspid area a systolic murmur could be heard, while at the aortic area a sharp systolic murmur was present and was carried through the aorta up to the arteries of the neck. The diastolic sound over the aorta was normal, while distinctly accentuated and reduplicated over the pulmonary artery. The liver was distinctly enlarged, extending 5 cm. below the costal margin, and was easily palpable. Pulsation of the liver, however, could not be made out. The urine was very scanty and contained a small amount of albumin.

The diagnosis was made of aortic stenosis, mitral insufficiency and stenosis, and tricuspid insufficiency.

Under large doses of digitalis the heart regained sufficient strength, the oedema, the cyanosis, and the albumin in the urine disappeared. Three days after beginning the digitalis medication the pulse frequency fell below 60; digitalis was stopped, but the frequency of the pulse kept on falling until on the fifth day it fell to 28; comparison

with the apex showed that each radial pulse corresponded to a bigeminal heart beat, of which the second was abortive.

The patient made an uneventful recovery. The tricuspid murmur disappeared with the slowing of the pulse. Six weeks afterward the patient left the hospital with a heart sufficiently compensated for light work.

At the beginning of January the patient returned for treatment, with almost the same condition that prevailed when he first entered the hospital. He reacted again very nicely to digitalis medication; under small continued doses of digitalis the heart has kept in good condition ever since.

Certain auscultatory phenomena at the time of the first examination attracted our attention to the possibility of dissociation between the action of the two ventricles. During the first few days the heart action was so rapid that no definite inferences could be drawn; as the heart began to slow down, however, it appeared that a certain number of the beats not leading to a radial pulse were distinctly different from the normal systoles and produced auscultatory phenomena very different from the usual cardiac sounds. While in successful contractions the first sound started with a clicking sound, indicative of mitral stenosis, in other contractions only a very soft systolic murmur could be heard followed by a normal second sound. The absence of the clicking sound seemed to show that the mitral orifice did not close and that, therefore, the left ventricle during certain phases of the heart action did not contract. Occasionally another modification of the heart sounds was observed: It seemed as if both the first and the second sound started an echo; the first sound was followed by another sound too far separated to be taken for a simple reduplication; then a second sound could be heard followed by another second sound.

Both these phenomena seemed to point to dissociation between the action of the right and the left ventricle; tracings taken at that time corroborated this view. Under the influence of digitalis these auscultatory signs disappeared entirely; the right and the left heart seemed to work together. Later on the dissociation recurred, but without any auscultatory signs indicating a dissociation. The most painstaking auscultations of the heart did not reveal any sounds, while the jugular vein still kept on pulsating.

A great number of tracings were taken during the four months the patient was under observation. The difficulty in arriving at an understanding of the waves present in the tracings obtained called for further observations; but at no time except at the time of the acute digitalis poisoning, could anything be obtained resembling a normal phlebogram.

Figs. 1, 2 and 3 are parts of tracings selected as best illustrating the condition constantly found. Fig. 1 was taken at slow speed, Figs. 2 and 3 at high speed, as may be seen from the markings corresponding to  $\frac{1}{2}$  seconds.

Fig. 1, taken at slow speed, demonstrates the impossibility of finding a definite relation between the arterial pulse and the jugular pulse. The heart is beating irregularly but slowly, as can be seen from the tracing of the apex beat; the radial pulse corresponds in

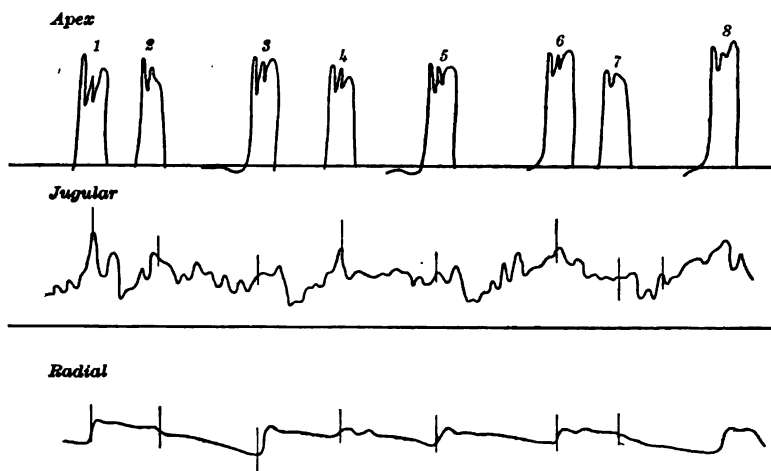


FIG. 1.—Taken at slow speed; the marks indicate the beginning of systole in the radial artery and the corresponding point in the venous pulse.

frequency to the apex beat. If two heart beats follow each other quickly, as systole 1 and 2, the radial pulse corresponding to the second beat becomes very small and is considerably retarded compared to normal beats. This is another illustration of the Extra-

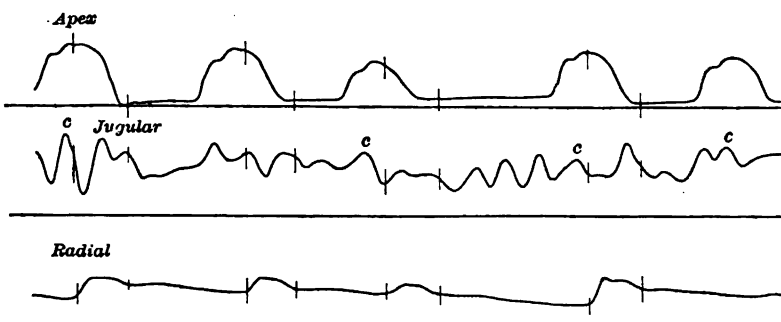


FIG. 2.—The same as Fig. 1, but at high speed.

verspätung described by Hering, due to the occurrence of premature beats. The heart muscle, which has not recovered sufficient strength in the short diastole, opens the aortic valves at a later period of the systole; the extra wave travels in the arterial system not as quickly as a normal wave, for reasons sufficiently discussed by Hering.

If one tries to analyze the venous pulse occurring between one apex and radial beat and the next, one is impressed by the number of waves corresponding to one heart evolution. In systole 2 there are seven waves occurring between radial beat 2 and 3; in systole 5 there are ten waves. Similar conditions prevail in Figs. 2 and 3, taken at high speed. In systole 3 of Fig. 3 there are five waves corresponding to one radial pulse.

The interpretation of the venous pulse offers great difficulties, since the normal waves of the venous pulse cannot be identified. In Fig. 3 corresponding points are marked, the first mark of each systole corresponding to the beginning of the radial pulse; the second mark shows the beginning of diastole indicated by the dicrotic wave. While the points on the apex beat and radial tracings correspond very nicely in the different systoles, no relation can be found between

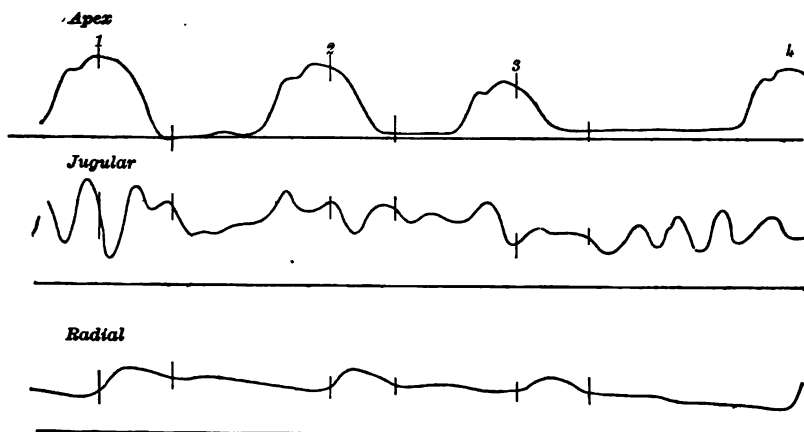


FIG. 3.—Taken at high speed; shows in systole 3, 5 venous waves corresponding to one arterial pulsation.

the waves of the venous pulse and the radial pulse. Sometimes the *c* wave corresponds to a very sharp wave, sometimes to a very slow wave, sometimes to a depression. In Fig. 3, systole 3, a diastolic wave is entirely missing, showing that the diastole of the right ventricle did not occur at the same time as the diastole of the left, thus proving the dissociation in the action of the two ventricles.

The explanation of the venous waves occurring during the diastole of the left ventricle is very difficult. Waves occurring during diastole known so far are: (1) The *v* wave occurring synchronously with the beginning of diastole. (2) The wave *a* produced by the contraction of the right auricle preceding ventricular systole. (3) Lately, A. Hirschfelder<sup>9</sup> has drawn attention to a wave *h* occurring

<sup>9</sup> Johns Hopkins Hosp. Bull., vol. xviii.

in diastole and caused, according to his interpretation, by the closure of the mitral valve. Gibson later described the same wave and connected it with a third heart sound which occasionally may be heard in a slowly beating heart. Einthoven has encountered the same wave in his electrodiagrams.

Four waves, therefore, may correspond to one arterial pulse: The *a* wave corresponding to auricular systole; the *c* wave due partly to the transmitted carotid wave, and partly to a systolic venous wave; the *v* wave setting in at the beginning of diastole; and the *h* wave occurring in full diastole, and the cause of which is still under discussion.

To one evolution of the left ventricle only four venous waves can possibly correspond. The recurrence of seven to ten waves during one arterial pulse can be explained in one of the following ways: (1) In case the waves are caused by contraction of the auricle, (a) by block between the auricle and the ventricle, and (b) by fibrillations of the auricles. (2) In case the waves are ventricular in origin, by dissociation between the action of different parts of the ventricle. To decide which of these explanations should be adopted, tracings of the heart action were taken from the oesophagus; at the same time

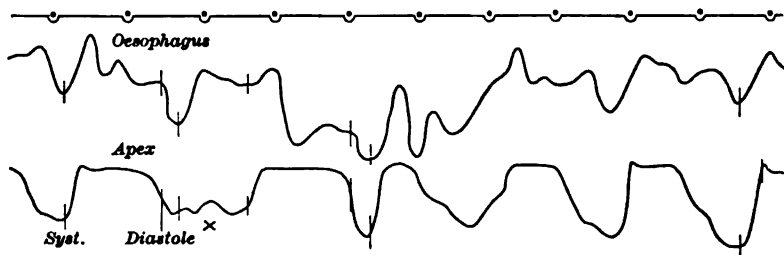


FIG. 4.—Oesophageal cardiogram.

the apex beat was registered (Fig. 4). To understand the meaning of this tracing I must discuss the meaning of the normal oesophageal cardiogram, the explanation of which we owe to Rantenberg<sup>10</sup> and Hewlett.<sup>11</sup> Fig. 5 is taken from Rantenberg's work. The wave preceding the apex beat is evidently due to the action of the left auricle as *s*; at the beginning of the ventricular systole the oesophageal tracing also shows a raising line *vs*, followed by several secondary waves, until the beginning of diastole is indicated by a sudden sharp fall *D*. At this moment the diastole begins and the mitral valves open; the left auricle which is in contact with the registering apparatus suddenly collapses, leading necessarily to a sudden fall of the tracing.

<sup>10</sup> Archiv. f. klin. Med., 1907, xci.

<sup>11</sup> Jour. Med. Research, 1907, xi.



These points, applied to the interpretations of the œsophageal tracing obtained in my case, show that the œsophageal registration concords absolutely with the cardiogram. The number of beats registered corresponds with the number of apex beats, and not with the venous tracings. On the other hand, no trace of auricular contraction could be obtained, proving that in this case the irregular heart action was complicated by auricular paralysis, as was to be expected in a case of perpetual irregularity.

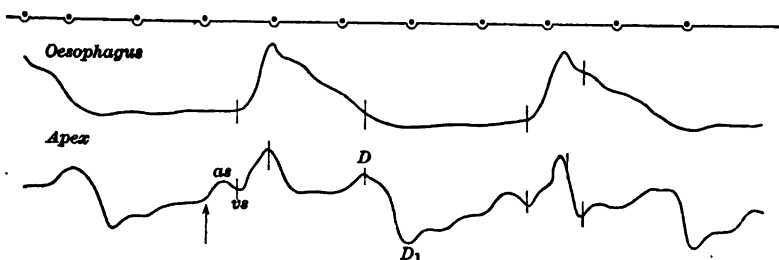


FIG. 5.—Normal œsophageal cardiogram.

On the other hand, the absence of auricular waves proves that the right auricle was paralysed. We know from the work of Fredericq and Erlanger,<sup>12</sup> that the left auricle is almost invariably dependent upon the right auricle for its activity. Fibrillation of the right auricle with complete paralysis of the left auricle has never been observed, as far as I have been able to learn; the same reason also excludes the possibility of block between the auricle and the ventricle.

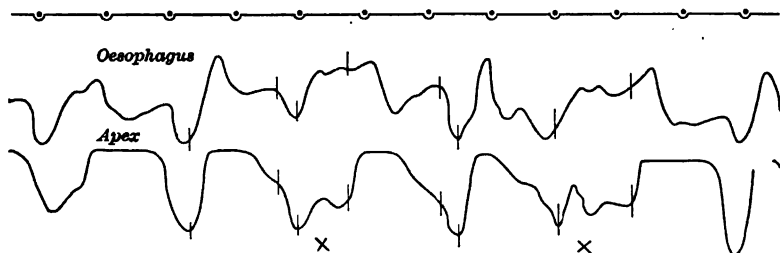


FIG. 6.—Showing partial contractions of the left ventricle at the points marked by X.

I am, therefore, obliged to assume that the multiplicity of the venous waves is due to dissociation in the action of the right and the left ventricle.

The mechanism of this dissociation is shown by the œsophageal tracing. In Fig. 6 two parts of the œsophageal tracings, together

with the corresponding apex beats, are reproduced. In the places marked by *X*, there are three instances in which both apex and œsophageal tracing differ quite distinctly from the other parts of the tracing. In both, following the fall which marks the beginning of diastole, there is a new ascending wave, corresponding in the apex tracing to a beat very much smaller in size than the usual apex beat. In the œsophageal tracing the wave due to this contraction seems to be slightly smaller than the usual wave: the principal difference from the ordinary beat, however, is due to the fact that the next beat begins before the fall of the curve indicating that the beginning of diastole has set in. In other words, the next contraction begins before the previous contraction has finished. This can take place in two ways: (1) In the form of partial contraction of the ventricle;

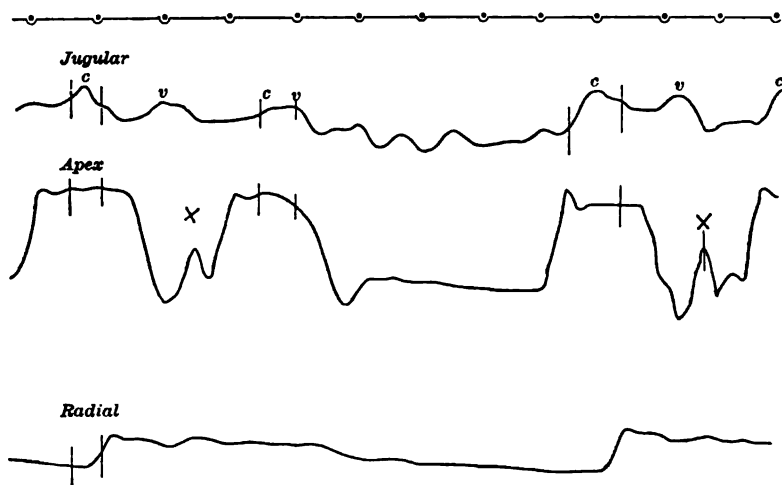


FIG. 7.—Showing at the points marked *X* partial contractions of the left ventricle interrupted before diastole by a complete systole.

that only one part of the whole ventricle responds to one stimulus, another part to a subsequent stimulus. (2) Another explanation may be found in the possibility that under certain conditions the law of the refractory period of the heart muscle does not hold good, and that under certain conditions a superimposed contraction may occur in the already contracting ventricle.

While the second view may be discussed, in view of the work of Rhode and Carlson, showing that under certain conditions the heart in systole is not absolutely refractory to new stimuli, such a supposition would not be justifiable in view of Fig. 3, which shows an absolute incongruence in the work of the right and the left ventricle. We, therefore, have to admit as an explanation the occurrence of partial contractions of the ventricles. It has to be conceded that such partial contractions do not occur only in the right ventricle; the

oesophageal tracings showed that similar partial contractions occurred also in the left ventricle. Fig. 7 shows also at the point *X* a partial contraction interrupted before its diastole by the following full-sized diastole.

I have already proposed the name of ataxia of the heart muscle for the phenomenon of partial ventricle contractions. As in locomotor ataxia the coordination of the different parts of the muscles of the limbs has been lost, so in ataxia of the heart the cooperation of the different parts of the heart muscle is lost. How the circulation can be kept up effectively under such conditions is a marvel to anybody who has carefully analyzed the action of such a heart. Evidently the partial contractions do not influence the blood stream which is entirely kept up by the full-sized contraction.

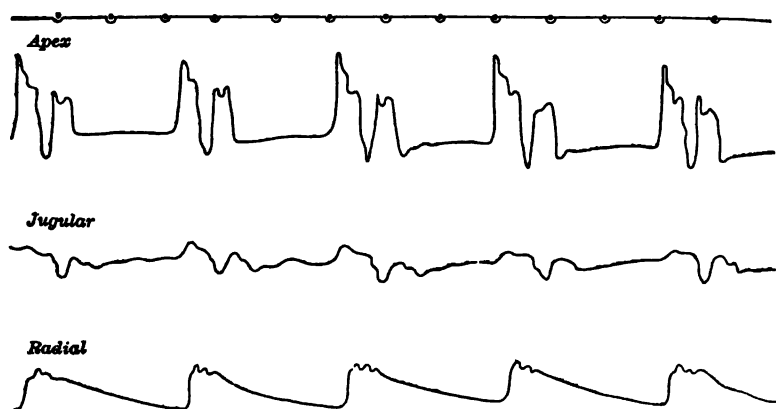


FIG. 8.—Showing typical digitalis action with normal phlebogram of ventricular type without any partial contractions.

The explanation of the phenomenon of ataxia is very difficult. One could at first think that the stimulus originating at the auriculo-ventricular ring is blocked in different places and reaches different places of the ventricle at different times. Such an explanation is impossible in view of the fact that the ataxia of the heart disappeared under digitalis (Fig. 8). Digitalis slows conduction and would aggravate any condition due to a lesion of conductivity. I believe the phenomenon to be due to different parts of the heart originating their own rhythm, as shown in Erlanger's experiments, in which every part of the heart muscle, even if separated from the region of the large veins or the His bundle, contracted rhythmically.

Investigation of ataxia of the heart will certainly show that partial contractions of the ventricle occur quite frequently in perpetual arrhythmias, and that a large number of symptoms observed in these cases can be explained only by partial contractions of the ventricles.

THE INTERPRETATION OF THE VENOUS PULSE.<sup>1</sup>

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THE knowledge of the existence of pulsations in the veins dates back to 1704 when Homberg<sup>2</sup> presented to the French Academy the result of his observations on the venous pulse. Morgagni,<sup>3</sup> however, was the first to offer rational views concerning this phenomenon. His dissertation upon the venous pulse is to be found in his work, *De sedibus et causis morborum*, which appeared in Venice in 1762. The first attempts to study the venous pulse experimentally were made by Barry<sup>4</sup> in 1826 and by Wedemeyer<sup>5</sup> in 1828, but owing to the inadequate methods used, their results were rather unsatisfactory. Bamberger<sup>6</sup> in 1856, and others following him, in common with their clinical predecessors, described the venous pulse as occurring only in tricuspid insufficiency. Bamberger, later (1863) published tracings of the venous pulse of tricuspid regurgitation, while Marey<sup>7</sup> in the same year took graphic records from animals. Friedreich,<sup>8</sup> in 1865, showed its presence in conditions other than tricuspid insufficiency, and described it as being formed of two waves: one presystolic in time and due to the contraction of the auricle, the other systolic in time and due to the shock of the aorta against the superior vena cava. Potain,<sup>9</sup> in 1868, described the venous pulse as composed essentially of a positive wave, due to the auricular systole, followed by two negative waves, the first being caused by the auricular, the second by the ventricular diastole. The same observer, in 1881, published tracings taken simultaneously from the jugular vein, and either the carotid artery or the cardiac apex. In the same year Riegel<sup>10</sup> interpreted the normal venous

<sup>1</sup> Read by invitation at a meeting of the Pathological Society of Philadelphia, April 9, 1908.

<sup>2</sup> Sur un battement de veines semblable au battement des artères. Hist. acad. roy. d. sc., Paris, 1704. Amst. 1707, 218 to 223. Also, Rec. d. mem., Dijon, 1754, ii, 138 to 140.

<sup>3</sup> De sedibus et causis morborum, Venice, 1762. Letter XVIII, Sec. 9, 10, 11.

<sup>4</sup> Recherches expérimentales sur les causes du mouvement du sang dans les veines. Mem. Acad. d. Sc., Paris, June 8, 1825. Paris, chez Crevot, 1825. Experimental researches on the Influence of Atmospheric Pressure upon the Progression of the Blood in the Veins, etc., London, T. and G. Underwood, 1826.

<sup>5</sup> Untersuchungen über den Kreislauf des Blutes und insbesondere über die Bewegung desselben in den Arterien und Capillargefäßen, Hanover, 1828.

<sup>6</sup> Lehrbuch der Krankheiten des Herzens, 1857. Beobachtungen über den Venenpuls. Wüstab. med. Ztschr., 1863, iv, 232.

<sup>7</sup> Physiologie méd. de la circulation du sang, 1863.

<sup>8</sup> Ueber den Venenpuls. Deut. Arch. f. klin. Med., 1865 to 1866, i, 241.

<sup>9</sup> Des mouvements et des bruits qui se passent dans les veines jugulaires. Mem. soc. med. hop. de Paris, 1867 and 1868.

<sup>10</sup> Ueber den normalen u. pathologischen Venenpuls. Deut. Arch. f. klin. Med., 1882, xxxi, 1. Experiment. Untersuchungen über den normalen Venenpuls, Deut. Arch. f. klin. Med., xxxi, 470.

pulse very much as Friedreich had before him, believing, however, that the principal wave was that originating in the contraction of the auricle.

Since that time most of the descriptions given in text-books on diagnosis, have embraced two forms of venous pulse: (1) The physiological venous pulse, characterized by a presystolic positive wave attributed to the arrest or slowing of the flow of the blood in the veins as a result of the auricular contraction; since this wave is immediately followed by a negative wave synchronous with the arterial pulse, this form of venous pulse is sometimes called systolic venous collapse; (2) the pathological or centrifugal regurgitant venous pulse consisting of a systolic positive wave due to a regurgitation of the blood into the auricle, and, possibly, also into the veins during ventricular systole and characteristic of tricuspid insufficiency, whether it be organic or functional.

François Franck<sup>11</sup> and later Fredericq,<sup>12</sup> showed that in the absence of tricuspid regurgitation a slight systolic wave is constantly present in the jugular veins of animals. Franck attributed the formation of this wave to the shock of closure of the auriculoventricular valves, while Fredericq believed it to be due to the sudden projection of these valves into the auricle at the beginning of ventricular systole. They both interpreted the presystolic wave as their predecessors had: as caused by the auricular systole. They also called attention to a third wave occurring at the end of ventricular systole. François Franck ascribed it to the sudden lowering of the base of the heart at this phase of its cycle. Fredericq assigned its cause to the sudden diminution in volume of the auricle occurring when its walls return to their position of rest.

To Mackenzie<sup>13</sup> belongs the credit of having attracted the attention of clinicians to this third wave, which had escaped their notice until his excellent work, *The Study of the Pulse*, appeared.

The apparatus used to obtain the tracings shown in this article consists of two Marey tambours provided with long levers made of very thin, light straw, the writing points being short and thin strips of aluminum. The pulsations were taken up by means of Mackenzie's capsule, or by means of a small glass funnel, according as the one or the other gave the better results. So far as the venous pulsation is concerned, Mackenzie's capsule with a flat side which can be laid against the clavicle, is best adapted for the purpose. Needless to say, the rubber tubes leading from the receivers (capsules

<sup>11</sup> Mouvements des veines du cou en rapport, etc. *Gas. hebdomadaire de médecine et de chirurgie*, Mars et Avril, 1882. Nouvelles recherches sur un cas d'ectopie cardiaque pour servir à l'étude du pouls jugulaire, *Arch. de phys.* 1889, i, p. 70.

<sup>12</sup> Sur le pouls veineux physiologique, *Travaux du laboratoire*, 1889 to 1890, t. iii, p. 85. La pulsation du cœur chez le chien. *Arch. de biologie*, 1890, x.

<sup>13</sup> The Significance of the Venous Pulse. *Edinb. Med. Jour.*, 1894. *The Study of the Pulse and Movements of the Heart*, London, Macmillan, 1903. *The Interpretation of the Pulsations in the Jugular Veins*. *AMER. JOUR. MED. SCI.*, 1907, cxxxiv, 12.

or glass funnels) to the tambours were exactly of the same length. Especial care was also taken before each observation to see that the writing points fell exactly on the same perpendicular line. The kymograph, on which the records were made, is the latest model of the Harvard kymograph, the speed of which can readily be varied to suit each particular case. The time record was obtained by means of a Page vibrator, the reed of which vibrated fifty times a second.

The superiority of such an arrangement is obvious when one compares the results here presented with the tracings taken with even the best of the small sphygmographs. The clockwork of the latter instruments is often too slow to permit of an accurate estimation of slight differences of synchronism between two curves, a point which is not without importance, as we shall see later.

The venous pulsation was taken from the point at the root of the neck which gave the best excursion of the lever. In the great majority of instances this point is to be found on the right side, although in a certain number of cases the venous pulse is more marked on the left side. The best pulsating point is often over the position of the jugular bulb, but it is by no means rare that a better jugular pulse can be recorded when the receiver is placed over the lower part of the external jugular vein. Finally the patient was placed in the recumbent posture, for in many cases the jugular pulse disappears when the patient assumes a posture in which the trunk is erect. As dyspnoea is a disturbing factor, whenever this was present the patient was asked to breathe as quietly as possible.

For the purpose of timing the various events in the complete cycle of a jugular pulsation, a simultaneous record of an arterial pulse or of the heart beat is indispensable. The carotid pulse was, therefore, taken simultaneously with the jugular pulse, and in all those cases in which it was possible a record of the heart beat was also taken simultaneously with the jugular pulsation. In order to establish points of synchronism in the two curves, ordinates were drawn with the levers while they were still in the position they occupied during the time the tracing was being taken.

In Fig. 1 the complete cycle of a jugular pulsation is seen to consist of three positive waves, the first two of which, *a* and *s*, are relatively of short duration and have a sharp summit, while the third wave, *v*, is of longer duration and has a broad summit divided by a notch so that it presents a bifid appearance. These positive waves are separated by three depressions, or negative waves. The first two (*2* and *Af*) are abrupt and occupy little time, while the third (*Vf*) situated between wave *v* and the next jugular pulsation, is more gradual in its descent, is deeper, and occupies a longer time in the cycle.

The first positive wave, *a*, is presystolic in time and is invariably interpreted as being due to the contraction of the auricle. The

mechanism of its causation, however, admits of several interpretations. It may be due to the slowing or arrest of the venous flow with a resulting damming of the blood and increase in the diameter of the veins, or to the suddenness with which the blood stream is stopped, this giving rise to a wave travelling in a reverse direction. It may also be due to the propagation of a wave of regurgitation from the auricle.

Certain investigators, as Fredericq and Nuel,<sup>14</sup> do not believe that any regurgitation occurs in the great veins during auricular systole, under physiological conditions. On the other hand, Chauveau and Faivre<sup>15</sup> state, that in the horse there is normally a

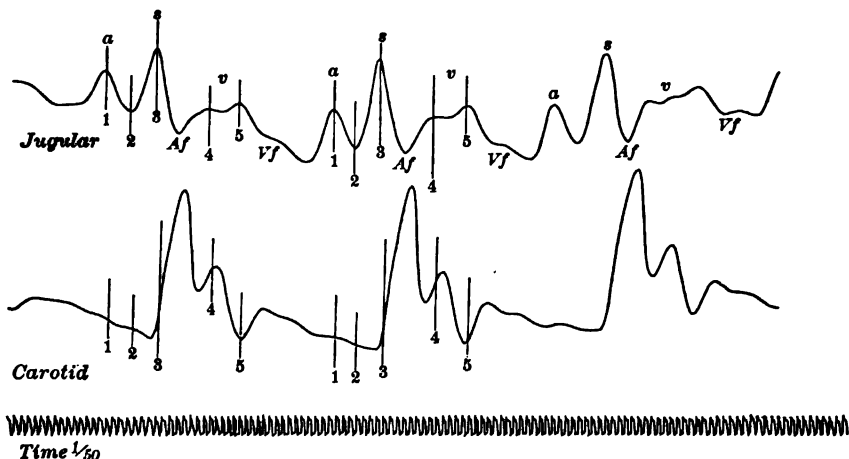


FIG. 1.—Simultaneous tracings of the jugular and the carotid pulses. From a case of mitral insufficiency and stenosis with perfect compensation. (Was admitted in the hospital for hydrops of the gall-bladder.) *a*, auricular wave; *s*, systolic wave; *v*, ventricular wave; *Af*, auricular filling; *Vf*, ventricular filling. The ordinates having the same numbers mark synchronous points on the curves. The letters and numbers have the same significance in all the tracings.

slight regurgitation of blood into the great veins during the contraction of the auricle. Keith<sup>16</sup> advances the opinion that the mouth of the superior vena cava is normally closed during the systole of the auricle by the contraction of a muscle band, the *tinea terminalis*, which performs the function of the venous valves found in the hearts of reptiles and batrachians. Should the auricle become engorged, however, the relaxation of this muscle band would allow of regurgitation into the veins, and Mackenzie thinks that it is easily rendered incompetent by changes affecting the tonicity of the auricle.

<sup>14</sup> *Elements de physiologie humaine*, Gand, 1893.

<sup>15</sup> *Nouvelles recherches experimentales sur les mouvements et les bruits normaux du coeur, envisagés au point de vue de la physiologie médicale*. *Gaz. med. de Paris*, 1856, iii série, t. xi, p. 406.

<sup>16</sup> *The Evolution and Action of Certain Muscular Structures of the Heart*. *Lancet*, February 27, 1904 and March 5, 1904.

It is probable, however, that in the normal state the main factor in the formation of this wave is to be found in the slowing of the venous current, and the resulting accumulation of the blood in the veins, and, possibly, also in the production of a centrifugal wave originating through the sudden arrest of the inflowing blood.

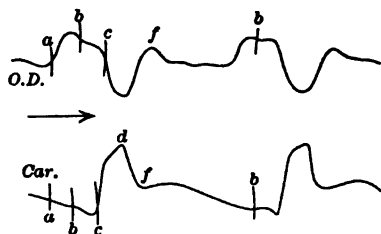


FIG. 2.—Simultaneous tracings of the intra-auricular pressure (*O.D.*) and of the pressure in the carotid artery (*Car.*) of a dog (morphine anesthesia). (Fredericq.) *a b*, auricular systole; *b c*, beginning of ventricular systole and projection of the auriculo-ventricular valves toward the auricle; *c d f*, outflow time; *f*, closure of semilunar valves (dirotic notch).

The negative wave seen between *a* and *s* is easy of explanation. It is due to the collapse of the veins occurring with the resumption of the flow of the blood consequent on the relaxation of the auricle. This fall in the curve is, however, quickly interrupted by the positive wave, *s*, the interpretation of which has given rise to a great deal

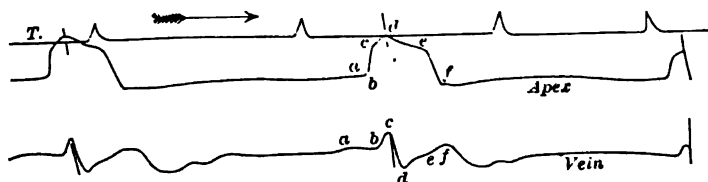


FIG. 3.—Simultaneous tracings of the apex beat and of the jugular pulse obtained from a large dog (morphine anesthesia). (Fredericq.) *a b*, auricular systole; *b c*, beginning of ventricular systole and projection of the auriculo-ventricular valves toward the auricle; *c d e*, (on apex tracing) systolic plateau; *e*, closure of semilunar valves; *e f*, relaxation of ventricles; *T*, time in seconds.

of controversy. It will be noticed that it is systolic in time, more correctly protosystolic, for it is normally synchronous with the beginning of ventricular systole. It reaches its height in the interval comprised between the beginning of the contraction of the ventricle and the opening of the semilunar valves, in other words, in that part of the cardiac cycle designated by the French as "*systole préparatoire*," and by the Germans as "*Verschlusszeit*" (Figs. 2, 3, and 4).

This wave was formerly considered abnormal and as being due to tricuspid regurgitation. This has been shown to be incorrect, as the jugular veins of normal animals exhibit it. Several explana-



tions have been offered concerning its mode of production. Friedreich attributed it to the impact of the aorta against the superior vena cava. As already stated, François Franck believed it to origi-

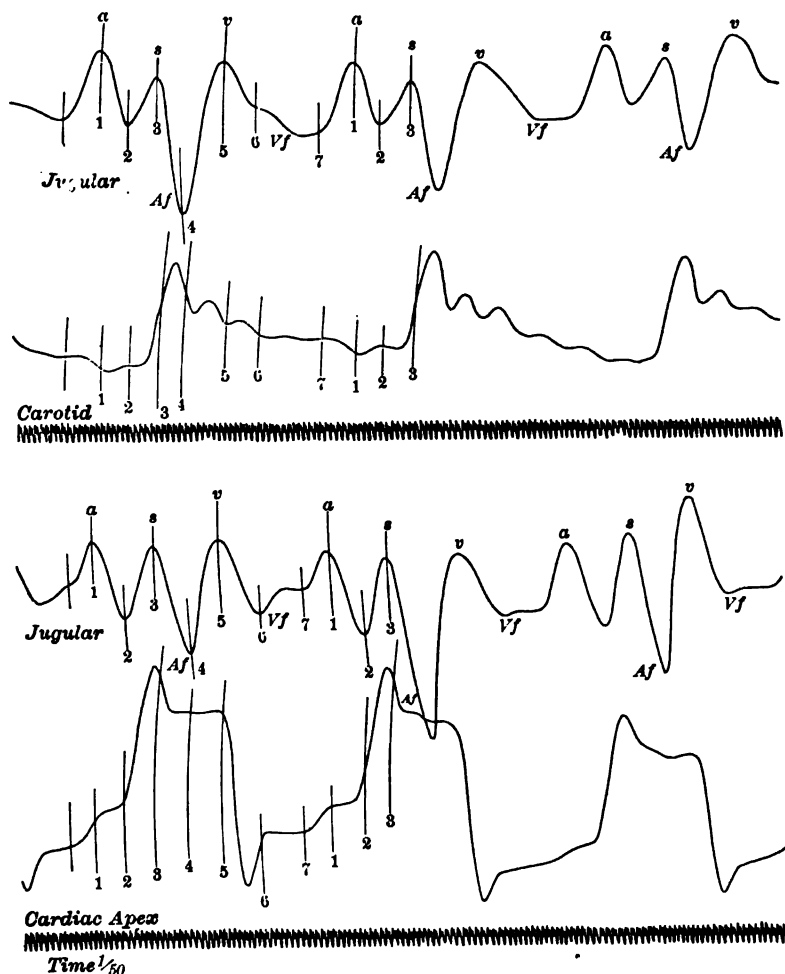


FIG. 4.—Simultaneous tracings of the jugular and the carotid pulses and of the jugular pulse and apex beat. Note that the upstroke of wave *s* coincides with the upstroke of the ventricular contraction (ordinate 2). Accordingly wave *s* precedes the carotid pulse by about 5/100 second. Wave *v* in this case is single. (Case of aortic regurgitation and relative mitral insufficiency with failing compensation.)

nate in the sudden closure of the tricuspid valve, while Fredericq thought it was due to the projection of these valves toward the cavity of the auricle. Gerhardt<sup>17</sup> does not think that this latter explana-

<sup>17</sup> Klin. Untersuchungen über Venenpulsationen. Arch. f. exp. Path. u. Pharm., xxxiv, 402. Einige Beobachtungen am Venenpuls, Arch. f. exp. Path. u. Pharm., 1902, xlvii, 250.

tion is warranted. He considers that the auriculoventricular opening is so tightly closed by the sphincter action of the ring of muscle around it, that as a result the valve leaflets are kept almost completely in apposition and that therefore they could not be pushed toward the auricular cavity by the sudden rise in ventricular pressure due to the contraction of the ventricle. He accordingly prefers Friedreich's explanation that the arteries coursing alongside the veins animate them with their own pulsation. Mackenzie adopted a similar interpretation, and he attributes the production of this wave as seen in the jugular pulse to the communicated impact of the neighboring carotid artery; hence the name he gave to it of "carotid wave." Mackenzie has advanced a number of arguments in support of his view. It is not within the scope of this paper to take them and discuss them seriatim. Those interested in the subject will find the necessary information in papers by Morrow<sup>18</sup> and by Bard.<sup>19</sup>

No one will dispute the fact, however, that the pulsation of a contiguous artery may contribute to the formation of this wave. However, I do not believe that it arises entirely from this source, but rather that it is independent of it, and that all the pulsation of a neighboring artery can do is to add itself to it, or vitiate it. Bard states that he obtained this wave from a vein in front of the clavicle and that it occurs in those cases in which the carotid is pulseless, provided the ventricles do not fail to contract. Animal experimentation has made this point clear. Fredericq, Morrow, Cushny and Grosh<sup>20</sup> and others have shown that this wave can be obtained when methods of recording the jugular pulse are used that do not involve pressure over the carotid artery, as well as when the vein is carefully dissected away from the artery, or when the carotid is clamped close to the aorta. The objection can be raised, however, that these methods do not eliminate the influence of the aorta on the vena cava. An examination of the curves of intra-auricular pressure obtained by Marey, Fredericq (Fig. 2), Porter<sup>21</sup> and others shows the presence of this wave in the position mentioned above. Porter ascertained that when the ventricle is inhibited by stimulation of the vagus, this wave does not appear in the curve; he therefore concluded that it is due to the pushing of the auriculoventricular diaphragm toward the auricular cavity. The venous tracings illustrating this article show a striking resemblance to the curves of intra-auricular pressure given by Porter in his valuable paper.

That wave *s* is really independent of any arterial pulsation is shown by the fact that, in the majority of cases, it precedes the systolic

<sup>18</sup> The Venous Pulse. Brit. Med. Jour., 1907, 777. The Various Forms of the Negative or Physiological Venous Pulse, *ibid.*, 1906, 1807.

<sup>19</sup> De l'enregistrement graphique du pouls veineux des jugulaires chez l'homme. Jour. phys. et path. gener., 1906, t. VIII. Des divers details du pouls veineux des jugulaires chez l'homme, *ibid.*

<sup>20</sup> The Venous Pulse. Jour. Amer. Med. Assoc., No. 15, xlix, 1254.

<sup>21</sup> Researches on the Filling of the Heart. Jour. Physiol., Cambridge, 1892, xiii, 513 to 553.

line of ascent of the carotid pulse. So far as I am aware, Bard was the first to direct our attention to this point. An examination of the tracings shown here will reveal the truth of this assertion. In order to demonstrate this the tracings must be taken on a kymograph revolving at a sufficiently rapid rate to bring into evidence little

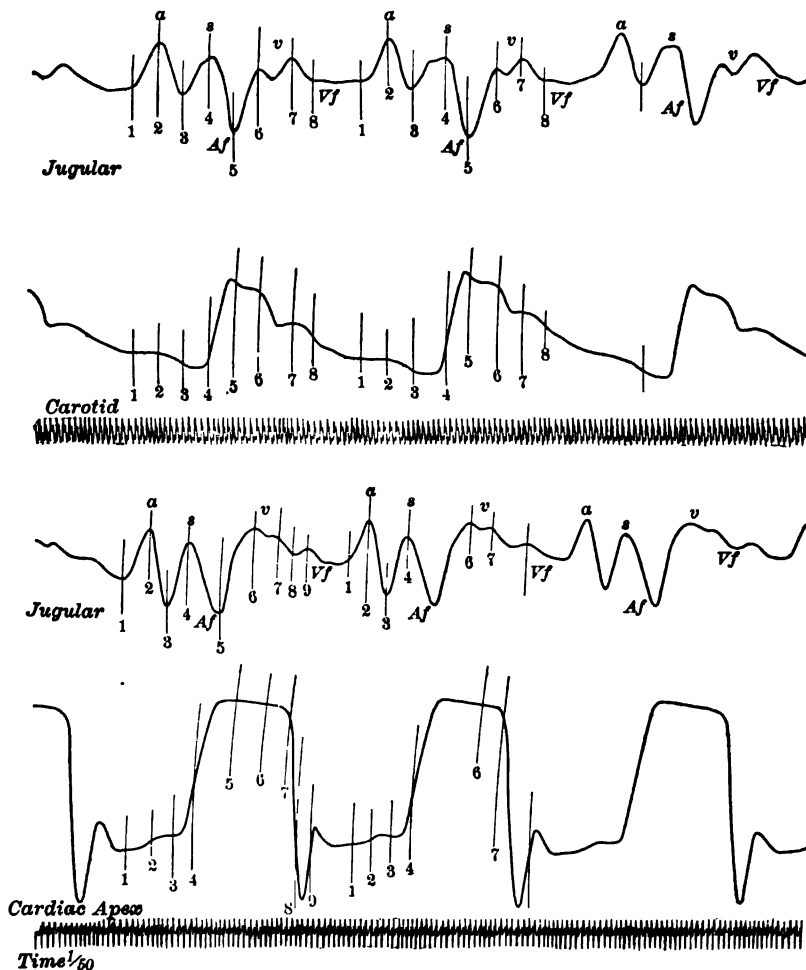


FIG. 5.—Simultaneous tracings of the jugular and the carotid pulses and of the jugular pulse and apex beat. From the same patient as Fig. 4 during a period of improvement.

differences of synchronism in the curves, and synchronous points should be marked with the levers in the manner already described, or by any other accurate method. The time elapsing between the beginning of wave *s* and the beginning of the carotid pulse varies in accordance with the degree of completion of the line of descent of the auricular wave, the rapidity with which the ventricle responds

to the stimulus coming from the auricle as well as the rapidity and ease with which the ventricle overcomes the pulmonic pressure. This is well exemplified in Fig. 6 taken from a case of mitral stenosis

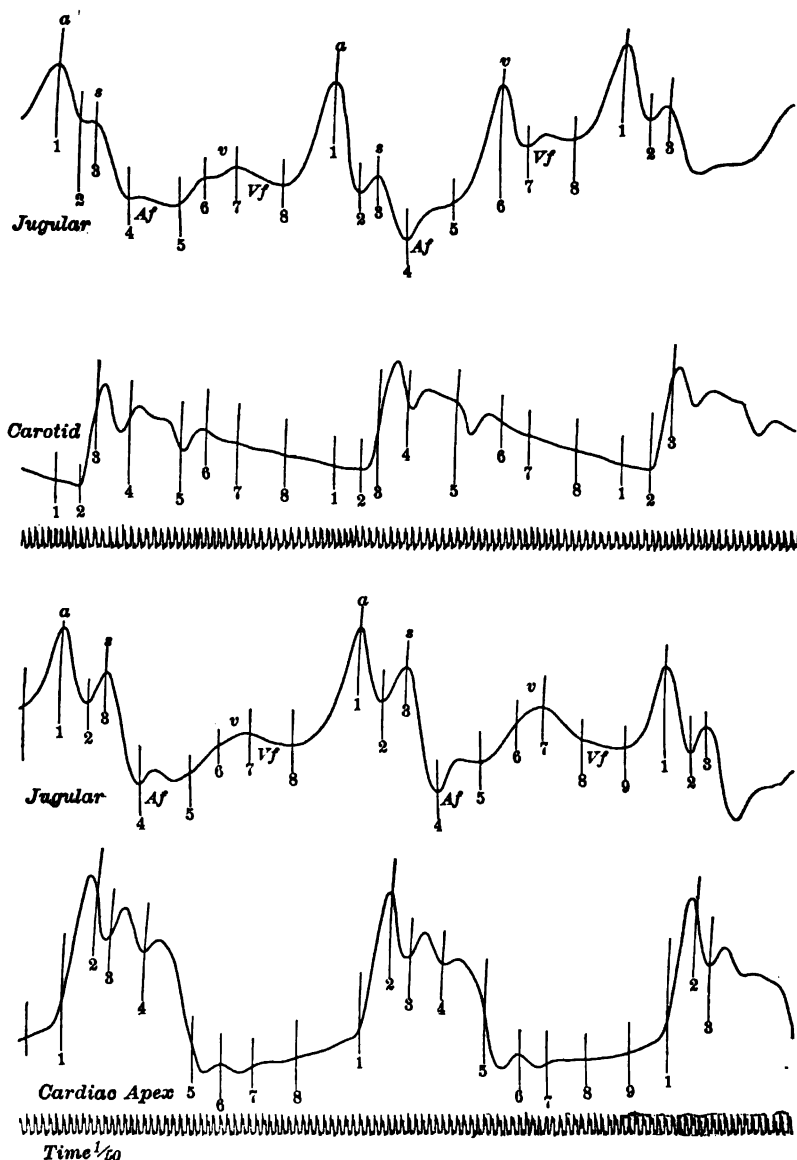


FIG. 6.—Simultaneous tracings of the jugular and the carotid pulses and of the jugular pulse and apex beat. Wave *v* occurs later in the cycle than in the other tracings. With the exception of the middle group, wave *s* begins with the carotid pulse. An examination of the lower tracings show that the ventricle responds quickly to the auricular impulse; wave *s* therefore occurs on the descending limb of wave *a*. (Case of mitral stenosis and regurgitation with beginning failure of compensation.)

in a fair state of compensation. According to Bard the difference in time between the appearance of this wave and the carotid pulsation, varies from  $\frac{1}{100}$  to  $\frac{2}{100}$  of a second. Until the present time, most of the tracings I have been able to obtain show somewhat higher figures,  $\frac{4}{100}$  to  $\frac{8}{100}$  of a second; in a few instances, however, Bard's figures were confirmed. In the middle group of Fig. 6, the time interval between ordinate 2 and the beginning of the carotid pulse is  $\frac{2}{100}$  of a second.

Following the protosystolic rise *s*, a sudden fall occurs in the tracing producing the negative wave *Af*. This wave is generally attributed to the rapid emptying of the veins which takes place during the diastole of the auricle. The negative pressure in the auricle is due, not only to the dilatation of its walls, but in great part also to the action of the contracting ventricle. Chauveau and Marey<sup>22</sup> observed that the auriculoventricular septum is displaced toward the apex during the systole of the ventricle, this having for effect an enlargement of the auricular cavity. Porter offered another explanation of the production of a negative pressure in the auricle based upon the investigations of Purkinje, Nega, and Roy and Adami. He believes that it is due to the contraction of the papillary muscles pulling the auriculoventricular valves toward the ventricle.

Some investigators have thought that this negative wave is caused by changes in intrathoracic pressure coincident with the change in the volume of the heart occurring during ventricular systole. Gottwalt<sup>23</sup> showed this conception to be incorrect, inasmuch as this negative wave persists even though the chest be opened.

This wave, then, is indicative of the filling of the auricle, and is the product of several factors: the expansion of the auricle, the downward movement of the auriculoventricular septum, and the pull exerted by the papillary muscles on the auriculoventricular valve leaflets. It begins with the opening of the semilunar valves and lasts until toward the end of ventricular systole, when the third positive wave makes its appearance.

The normal position of the third positive wave usually called ventricular wave, *v*, is toward the end of ventricular systole. However, different observers do not agree to this, and some, like Gerhart, believe it to occur during ventricular diastole. The fact is that the relation of this wave to the cardiac cycle is not perfectly constant, and that pathological conditions within the heart seem to influence both its position and its form. It is not the purpose of this paper to discuss the pathological modifications of the venous pulse; I shall, therefore, consider it only as it occurs normally in the jugular veins of animals, and in those human beings who exhibit venous

<sup>22</sup> Appareils et expériences cardiographiques, Mém. acad. med., Paris, 1863, t. xxvi, 313.

<sup>23</sup> Der normale Venenpuls. Arch. f. die ges. Physiol., 1881, xxv, 1.

pulsations either without apparent pathological cause or as a result of some slight venous embarrassment.

Various explanations have been offered concerning the interpretation of this wave. Some, like Rigel, think that it is due to the communicated shock of the arterial diastolic expansion; others, among whom is François Franck, see in it the effect of changes in intrathoracic pressure owing to the diastolic enlargement of the ventricle. But it has been shown that opening the thorax in animals does not affect the production of this wave. Mackenzie and others believe that it is due to the filling of the auricle and the consequent accumulation of the blood in the veins. Mackenzie, however, associates it in some way or other with tricuspid regurgitation.

While it is in all probability true that tricuspid regurgitation affects the *v* wave, it is none the less true also that it occurs in cases in which there is no regurgitation. It is found as a constant wave in the jugular pulse of animals, as well as in the curve of intra-auricular pressure. Moreover, the mechanism of its production is to be sought in the movements of the ventricle. Fredericq, Gerhart, Wenckebach, and others have ascribed it to the swinging back of the auriculoventricular septum. Morrow does not believe that the action of the ventricle is necessary for the formation of this wave, but Cushny and Grosh have shown that the suspension of the ventricular contractions is attended with the disappearance of this wave from the tracing.

It was stated above that two of the factors contributing to the formation of the negative wave *Af* are, on the one hand, the displacement of the auriculoventricular septum toward the apex, and, on the other hand, the pull of the papillary muscles on the tricuspid leaflets.

The relaxation of these papillary muscles and the return of the auriculoventricular septum to its former position decrease the cavity of the auricle, and, as the latter is filled, this encroachment upon its capacity has for effect an arrest of the flow and a damming of the blood in the veins. These two movements, however, are not synchronous, and, according to the researches of Roy and Adami,<sup>24</sup> the papillary muscles relax shortly before the beginning of ventricular diastole, hence before the return of the auriculoventricular septum to its position of rest. This relaxation occurs while the intra-ventricular pressure is still much higher than the intra-auricular pressure. We should, therefore, expect these two separate movements to be reflected in the wave under consideration. That this may be as here explained is seen by the constancy with which a notch is present on the summit of wave *v*, thus showing it to be made up of two lesser waves.

\* Heart Beat and Pulse Wave. Practitioner, London, 1890, xliv, 81, 161, 241, 347, 412; xlv, 20.

The variations in the form and in the position of this wave in the cardiac cycle are to be sought in pathological factors which may mask or annul the effect of the movements just described.

The third negative wave in the jugular pulse,  $V_f$ , occurs at the beginning of ventricular diastole, and is due to the opening of the tricuspid valve; the auricular blood entering the relaxing ventricle, the flow of the blood in the veins is accelerated, and the latter naturally decrease in diameter.

In almost all tracings taken from normal animals, either from the jugular vein or from within the auricle, this wave is more shallow than the negative wave  $A_f$  (auricular filling). Although the tracing of Fig. 5 was taken from a pathological case of aortic and mitral regurgitation, what may be taken as the normal ratio of the depth of these two waves is well shown there.

It seems at first strange that this negative wave should be so little marked, but if it be remembered that the base of the ventricle may still be continuing its upward movement, though perhaps more slowly, it will be easily understood how this would counteract the effect of the aspirating action of the ventricle by gradually decreasing the capacity of the auricle.

A slight positive wave is very constantly present at or near the trough of this negative wave. It is in all probability a wave of stasis due to the entrance of blood into the veins from the periphery.

A moment's consideration will make it apparent that the study of the venous pulse by the graphic method is destined to give valuable information concerning the pathological function of the heart, for it can reasonably be inferred from what has been said, that it mirrors, more faithfully than the arterial pulse, the events occurring within the heart. Already it has proved invaluable in the study of heart-block, and in the study of the various forms of arrhythmia.

**CONCLUSIONS.** The physiological or so-called negative systolic venous pulse consists of three positive and three negative waves bearing a more or less definite relation to the events of the cardiac cycle and having their origin in the various movements of the chambers and structures of the right heart. The first positive wave ( $a$ ) is presystolic in time and is due to the contraction of the auricle causing a slowing of the venous current and producing a centrifugal wave through a sudden arrest of the inflowing blood. The second positive wave ( $s$ ) is protosystolic in time and originates in the sudden projection of the tricuspid valve into the cavity of the auricle during the quick, incipient rise in intraventricular pressure occurring in the protosystolic period. The third positive wave ( $v$ ) occurs toward the end of ventricular systole. It consists of two lesser waves separated by a shallow notch. The factors entering into its formation are the relaxation of the papillary muscles at a time when the intraventricular is still higher than the intra-auricular pressure, this resulting in an upward movement of the

tricuspid leaflets, and to the return of the auriculoventricular septum to its position of rest.

The first negative wave (between positive wave *a* and *s*) is due to the relaxing auricle. The second negative wave (*Af*) occurs during the diastole of the auricle. It is due to the dilatation of its walls, to the displacement of the auriculoventricular septum toward the apex occurring at the time of ventricular systole, and to the pull of the papillary muscles on the tricuspid valve leaflets. The third negative wave (*Vf*) appears during ventricular diastole and in the common pause of the heart chambers. Its cause is found in the passage of the blood from the auricle into the ventricle. It is somewhat modified, possibly by the continued ascent of the auriculoventricular septum and by a wave of stasis due to the accumulation of blood coming from the periphery.

I wish here to thank Professors A. P. Brubaker and W. M. L. Coplin for their encouragement and advice, and Professors J. C. Wilson and H. A. Hare from whose wards the necessary material was obtained.

### FATIGUE IN SCHOOL CHILDREN AS TESTED BY THE ERGOGRAF.

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THE considerable number of children seen in dispensary service, particularly late in the winter and in the spring, suffering from nervous disorders, and the fact that these children are usually conscientious children who are making a desperate effort for a good showing at school, naturally leads one to suspect that school work is doing, at least some of the children, considerable harm. This feeling, I believe, is also shared by many school teachers.

Being interested in the physical welfare of the children in a large private school in New York, my attention was attracted to the work with the ergograph done under the direction of Dr. W. S. Christopher in the Chicago public schools during the years 1898, 1899, and 1900. Dr. Christopher was placed in charge of a department of child study, and undertook to apply various tests to the children so that each child might be so placed in school as best to acquire knowledge without physical harm. He tested the sight, hearing, lung capacity, etc. Among the various tests he applied to the children was a test of muscular activity, determined by the ergograph. The ergograph, which aims to use only one muscle and to exercise it until fatigue is produced, shows by comparative tests muscular fatigue. Dr. Christopher tested the children during various periods of the school day,



and found in a considerable number of experiments that there is a diminution in the physical activity as shown by the ergograph, commencing within an hour of the beginning of the school day and proceeding until the noon recess, after which about the same activity was shown as at nine in the morning, but it fell off again during the afternoon session. The report of 1899-1900 notes one exception to this rule, and that was in four boys, who, on questioning, stated "that their teacher had been called from school and that they had had no regular work, but had been sent to another room but employed themselves, as they said, in having a good time."

The amount of deterioration in muscular activity during the school day, as shown in these children, was on the average during the first experiments from 20 to 25 per cent. A later average of 1127 records of one school showed a morning loss of 16 per cent., and an afternoon loss of only 4 per cent. This slighter evidence of fatigue, in the afternoon might be attributed to the fact that the most difficult school work is now arranged in the morning curriculum.

These very valuable observations by Dr. Christopher were published, but, so far as I know, no practical application was made of them; that is, no attempt was made to work out a school day which might reduce or eliminate fatigue, for it has been well demonstrated that fatigue, as shown by the ergograph, is very marked fatigue, for after slight fatigue a better tracing may be obtained than with no fatigue.

It seemed to me probable that by the use of more frequent recesses such fatigue might be eliminated and a school day elaborated, which would be free from constant marked fatigue and would keep the children in a condition more favorable to the acquisition of knowledge and without physical harm.

My first efforts to measure fatigue in school children were undertaken at the Charlton School three years ago. Two tests for fatigue were then used: that suggested by C. Ward Crampton, of New York, which consists in obtaining the difference between the blood pressure of a child standing and in a horizontal position, and the rapidity of the heart action in a child standing and in a horizontal position. This test was used in combination with a test by an ergograph devised by Dr. Thomas A. Storey and kindly lent to me by Professor Lombard, of Ann Arbor, in which the abductor indicis was used; each movement of the index finger toward the thumb raising a weight and making a tracing on a kymograph. Throughout this work I have been much indebted to Professor F. S. Lee, of the department of physiology of the College of Physicians and Surgeons, of Columbia University, for his wise advice and for the laboratory facilities and laboratory apparatus put at my disposal.

With these two tests I used children who were first required to concentrate in their studies; that is, children of about seven years. Absolutely no appreciable evidence of fatigue was obtained from the

Crampton test of blood pressure and pulse rapidity, and no general fatigue such as that described by Dr. Christopher was obtained by the use of this ergograph. Although slight fatigue was usually shown by some children, no persistent marked fatigue was ever found in any class of children.

The following year I continued the same experiments with the same apparatus in older children at the Charlton School with similar results. One ambitious and conscientious girl of high standing, with an acute mind, who was anemic and poorly nourished, showed constant fatigue after her morning work. Some others showed occasional fatigue, others none.

Having worked for two years with very little result in this school I arranged during the past winter to conduct work in the public schools, and through the courtesy of Health Commissioner Darlington and Superintendent Maxwell of the Board of Education, and Superintendent Boyle, of Public School 69, I was enabled to obtain the facilities that I needed. I used for this purpose at first girls eleven years old, taking first a group of five whom their teacher thought were fatigued at the end of the school day. These children, who were apparently showing some fatigue, showed no marked fatigue such as Dr. Christopher observed in Chicago. Other groups of five children of the same age that were afterward taken gave similar results. I therefore concluded that further work with this ergograph was useless, either in order to confirm or obtain conclusions on the work done by Dr. Christopher.

I then procured a Mosso ergograph (Fig. 1), similar to the one used in Chicago, which was kindly lent to me by Professor Howell of Johns Hopkins University, and to this was attached an adder. This Mosso ergograph uses the flexor of the middle finger. It was arranged so that each flexion of the middle finger raises a weight, makes a tracing on the kymograph as well as registering the amount of work done on the adder. In the use of this apparatus the method followed in Chicago was adopted, each child pulling 7 per cent. of his weight thirty times a minute for one and one-half minutes, thus giving each child about forty-five pulls.

With this apparatus I have tested a considerable number of children in a New York public school and have obtained results exactly similar to those obtained with the other form of ergograph which I previously used. While some children show fatigue in their tracings after an interval of school work, other children will make better tracings than at the beginning.

Twenty children tested 9.30 A.M. showed an average of 264 kg. cm. of work; at 11.30, 286; at 1.30, 272, and at 3.30, 250. This shows a slight increase in muscular activity at 11.30 over 9.30 and again a slight diminution at 2.30 as against 1.30 (Fig. 2).

An average of 36 observations at 9.30 and 11.30 on both boys and girls from ten to fourteen years of age, gave an average result of 278

kg. cm. at 9.30 and 282 kg. cm. at 11.30, a slight increase in the amount done at 11.30 over 9.30. As some of these children were

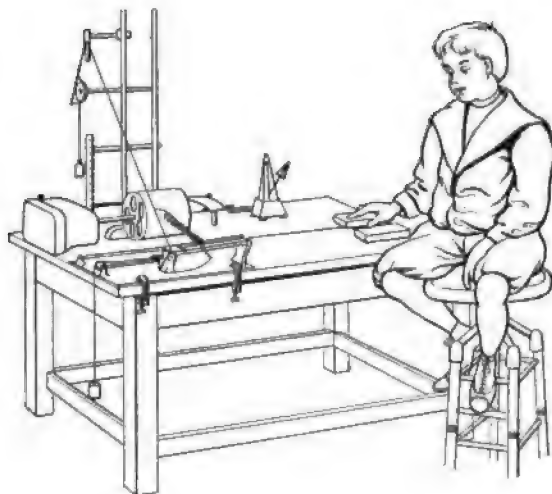


FIG. 1.—A child being tested with the Momo ergograph.

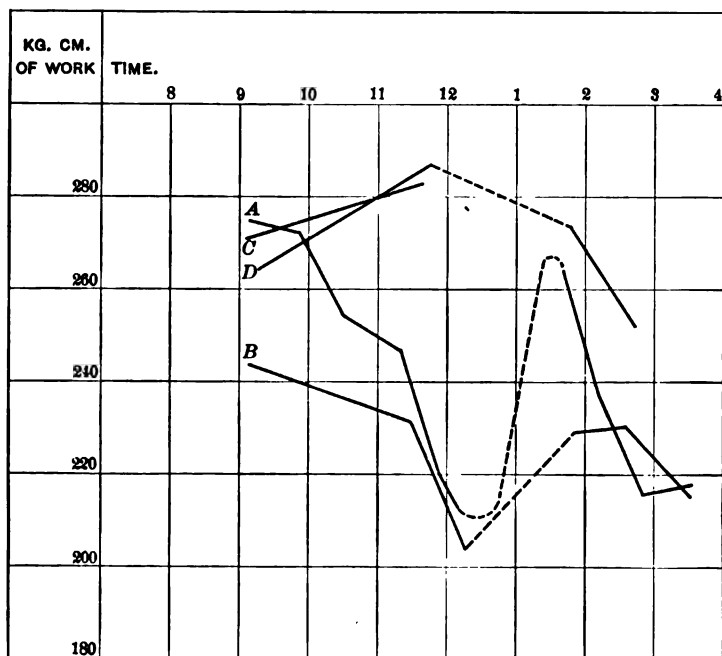


FIG. 2.—Influence of school work on physical activity. A, 8 Chicago public school children; B, 1127 Chicago public school children; C, 36 New York public school children; D, 20 New York public school children.

using the instrument for the first time on this day an estimate of the work done by children who had repeatedly used the ergograph might help to eliminate this possible error. Eleven children familiar with the instrument did an average of 204 kg. cm. of work at 9.30 and 256 at 11.30, so that there seems no way that we can use these figures to obtain results similar to those obtained by Dr. Christopher. This may be accounted for by a difference in the school curriculum. It is possible that the duties required of the pupils in Chicago are more difficult and that the sessions possess less opportunities for recesses. This would, of course, alter the results. As I have been unable to obtain the curriculum used in Chicago I cannot compare it with that used in New York.

As a conclusion, I might say that the Crampton test for fatigue has given negative results as applied to school children in New York; that the Storey ergograph as used for the detection of fatigue in school children has given negative results and is unsuitable on account of the use of accessory muscles when the abductor indicis becomes fatigued; that the Mosso ergograph combined with an adder as used in the Chicago public schools is the more reliable instrument for this purpose, but in my hands fails to give evidence of marked fatigue of the pupils during the school day in a private and also in a public school of New York City; and that in occasional children either form of ergograph will give evidence of fatigue.

The ergograph, so far as my work indicates, is of no value in modifying the school day in the public schools of New York for the average student, but might be shown to be of value in lightening and controlling the work for those pupils who give evidence of marked fatigue during the school day.

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### **THE DIAGNOSTIC VALUE OF CUTANEOUS HYPERALGESIA (HEAD'S ZONES) IN ABDOMINAL DISEASE.**

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ALTHOUGH fifteen years have passed since Henry Head first published his discovery of the association of increased sensitiveness of the skin with visceral disease, the literature of the subject has remained very small. Lange is said to have written about skin sensitiveness in visceral disease as early as 1871. Ross referred to

the subject in 1888, but Head was the first to make a careful study of the phenomena. Notwithstanding the importance of Head's publication, it seems to have attracted little attention outside of England. The papers of Mackenzie, Thorburn, Thane, and others, in England, and of Petren and Faber, on the Continent, are the only ones of importance that have appeared. In most of the text-books the subject has been dismissed with a few lines.

During the last two years we have made a large number of examinations in the wards of Mt. Sinai Hospital, to determine the presence or absence of areas of hyperalgesia in abdominal affections. The majority of the patients were admitted to the surgical service of Dr. Lilienthal, and were sooner or later submitted to operation, so that the results of our observations were verified by the operative findings. In the following paper are given the results of our studies, arranged under the following headings:

- I. Description of Head's zones.
- II. Methods to be used in testing for cutaneous sensitiveness.
- III. The appearance and disappearance of zones of hyperalgesia in abdominal disease.
- IV. The general significance of localized areas of cutaneous hyperalgesia in visceral disease.
- V. General consideration of the subject of hyperalgesic zones in abdominal disease.
- VI. Head zones in affections of the various viscera.
- VII. Conclusions.

#### I. DESCRIPTION OF HEAD'S ZONES.

In 1893 and later, Henry Head described certain definite and constant areas of cutaneous tenderness associated with diseases of the different viscera. He found that in many visceral affections, if the sensitiveness of the skin was tested by running a pin point over the cutaneous surface, there could be shown to exist areas over which there was a more or less marked hypersensitiveness to pain. As a result of painstaking investigations extending over many years, he concluded that these areas were constant and distinct; they could be mapped out on the surface of the skin, and, when present, were an almost infallible sign of an affection of the organ to which they corresponded. The skin tenderness was very superficial—quite different from tenderness on deep pressure—and extended over definite areas which never overlapped one another. Each area or "zone of hyperalgesia," as he called it, had a "maximum" region, which often corresponded to the location of the pain complained of by the patient, and coincided with the areas marked out by attacks of herpes zoster. Head found, also, that these areas were hypersensitive to heat and cold, but not to touch. He concluded that there is

an intimate association between the central connections for the nerves of the viscera and the nerves which supply the sensations of pain, heat, and cold, and those which exert trophic influences on the skin.

In his various publications, Head gave diagrams of the form and extent of these hyperalgesic zones. He showed that the areas corresponded to segments of the spinal cord, not to the distribution of peripheral nerves or spinal nerve roots or brain areas. Based on this segmental distribution, the zones were named according to the segments of the spinal cord: cervical, 1 to 7; dorsal, 1 to 12; lumbar, 1 to 5; sacral, 1 to 4. Head described the shapes of the zones, and stated that in general the zones were broader at the median line in front, became narrower at the side of the body, and again broadened out near the spinal column. The zones of each side never extended beyond the median line in front or behind.<sup>1</sup> Head stated, also, that there were individual differences in the form of the areas, but not in their general position, due to variations in the shape of the patient's body or in nerve supply.<sup>2</sup> For the abdominal viscera, Head gave the following zones:

Stomach, sixth, seventh, eighth, and ninth dorsal.

Cardiac end, sixth and seventh dorsal, right.

Pyloric end, eighth and ninth dorsal, left.

Liver, eighth, ninth, and tenth dorsal, right.

Gall-bladder, eighth and ninth dorsal, right.

Intestines, ninth, tenth, eleventh, and twelfth dorsal.

Colon, ninth, tenth, and eleventh dorsal.

Cecum and appendix vermiformis, tenth and eleventh dorsal, right.

Kidney, tenth dorsal, sometimes eleventh dorsal.

Ureter, eleventh and twelfth dorsal, first lumbar.

Bladder, (first?), second, third, and fourth sacral.

Uterus, tenth, eleventh, and twelfth dorsal, first lumbar.

Appendages, eleventh and twelfth dorsal, first lumbar.

To explain these areas of referred cutaneous hyperalgesia, Head proposed an hypothesis, which we here give in his own words:

"Why is the skin tender in consequence of visceral disease?

"If impulses pass up the sensory nerves from an organ which is diseased to the cord, they will set up a disturbance in the segment of the cord to which they are conducted. Now, any second sensory impulse from another part conducted to the same segment of the cord will be profoundly altered. Under normal circumstances, it would have set up its own proper disturbance in the gray matter,

<sup>1</sup> In a few instances we have observed that the areas extended slightly across the median line in front. This can be explained on the basis of nerve filaments from one side supplying the skin a little beyond the median line.

<sup>2</sup> The outline of the zones, as determined by us, sometimes varied somewhat from Head's diagrams (see below).

and this disturbance would have been conducted to the brain. But now it no longer falls into a normal and quiescent cord, but into one whose activity is already disturbed. The resultant stimulus conducted upward is therefore a very different one from that which would have passed on under normal circumstances. In many cases the second stimulus will be exaggerated like rays passing to the eye through a convex glass. Thus, if any segment of the cord is disturbed by painful stimuli from an internal organ, a stimulus applied to the skin over the areas supplied by the nerve roots belonging to this segment will be exaggerated, and a stimulus which normally was perhaps only uncomfortable would now appear to be very painful.

"But in order that this condition may result, the central nervous connection between the sensory nerves from the viscera must be closely connected with that part of the cord into which the sensory stimuli from the skin are conducted. We never find cutaneous hyperesthesia or increased sensitiveness to touch as the result of visceral pain, but only increased sensitiveness to pain or hyperalgesia."

## II. METHODS OF EXAMINATION.

No satisfactory and practical form of algesimeter for testing cutaneous hyperalgesia has thus far been devised.<sup>3</sup> Head tested the skin sensitiveness to pain by pinching up folds of skin, or, later, by stroking the skin with the point of a sharp pin. We have made use of the pin method, and have found it satisfactory for practical purposes. A sharp pin is held between the thumb and index finger of the right hand, the nail of the index finger resting on the patient's skin. The pin is then made to traverse slowly the surface of the skin, care being taken that the nail of the index finger presses equally along the area examined. The patient is instructed to say "now" as soon as the pin stroke becomes painful.

In examining the skin of the abdomen for hyperalgesic areas, the pin traverses the abdomen from side to side and from above downward; the points at which the patient complains of pain are marked. In this manner it is possible to map out areas on the skin, and when such an area has been found, the pin is made to approach it from all sides, so that its form and position can be determined. Care must be taken that the pressure of the pin point remains constantly the same, especially as the pin passes over the groin and slips off the costal border or over the crest of the ilium.

After the zone has been thus mapped out on the skin the procedure is repeated a second time, and now it is a good plan for the operator to control both patient and himself by keeping both the patient's

<sup>3</sup> The instrument described by Thudicum is not practical.

and his own eyes away from the pin. There is considerable variation in the sensitiveness of different persons; some will complain of pain with a pressure which others will hardly feel. It is therefore of advantage first to gain an idea of the general sensitiveness to pain of the patient.<sup>4</sup>

The hyperalgesia is sometimes so marked that the patient will shrink or cry out as soon as the border of the zone is reached. At other times one depends on the statements of the patient.<sup>5</sup> In very young children, the examination is useless, but older children will give correct answers.

If the examination is carried out in the manner above described, it will be possible in a large number of patients with visceral affections to map out areas of hyperalgesia extending from the median line in front to the spines behind. We have succeeded in substantiating most of the statements made by Head in regard to the zones of referred cutaneous hyperalgesia in abdominal disease. The "maximum" areas can often be mapped out lying within the boundaries of the zones; sometimes only the "maxima" are present. We have sometimes found several "maxima" in one zone.<sup>6</sup>

A certain amount of experience is necessary before satisfactory results can be obtained, and this experience must be gained by frequent careful tests for cutaneous hyperalgesia. We have found, with increasing experience, an increasing number of positive cases.<sup>7</sup>

### III. THE APPEARANCE AND DISAPPEARANCE OF ZONES OF HYPERALGESIA IN ABDOMINAL DISEASE.

The zones appear early in the course of visceral affections, and usually persist throughout the course of the disease. They disappear at once with the relief of the lesion. They may appear very early. Thus, in the very beginning of acute appendicitis, when the pain is still in the epigastric region, and there is no tenderness as yet in the right iliac region, there may be a well-marked appendix zone. The zones may appear after palpation, when they were not present before. Thus, we have seen the characteristic

<sup>4</sup> For this purpose we have sometimes found a test proposed by Dr. Libman of value. If one makes pressure with the thumb over the styloid process in the neck, one may gain a fair idea of the degree to which an individual is sensitive to pain. Some patients will complain of the slightest pressure, in others a considerable degree of force is required. (Personal communication through kindness of Dr. E. Libman, adjunct physician to Mt. Sinai Hospital.)

<sup>5</sup> It is often a good plan to control the patient's statements by testing the skin near the spine on the side opposite to that on which the zone has been found. This is, of course, done without the knowledge of the patient.

<sup>6</sup> Although, in front, the hyperalgesia may extend only over a small "maximum" area, the examination of the skin of the back should never be omitted. There may be a sensitive area posteriorly which will make the identification of the zone more certain.

<sup>7</sup> Thus, in the beginning of our investigations we were able to demonstrate zones of hyperalgesia in about 25 per cent. of cases of appendicitis; after some experience we have found "appendix zones" in almost 75 per cent. of the patients.



zone for the appendix appear after palpation of the right iliac region in acute appendicitis, and we have observed the zone for the uterine adnexa appear after a bimanual examination. Head states that, in one of his patients, after rough manipulation of a floating kidney, a "kidney zone" appeared.

In a few instances, we have been able to note the appearance of the zone while the patient was under observation. In these cases the zone usually appeared in its entirety. The presence of an ice bag, a hot-water bag, or a poultice may make it impossible for the examiner to map out the sensitive area, but if the ice bag or hot-water bag is removed, the hyperalgesic zone will appear after about fifteen minutes. Therefore, it is imperative to wait a short time after an ice bag, etc., has been removed before the examination is made.<sup>8</sup>

The disappearance of the zones is a question whose significance is often difficult of explanation. In general it may be stated that a prompt disappearance of the zone follows relief of the lesion of the affected viscus. We have, in a number of patients, been able to watch the disappearance of the zones. In some cases, the zone disappeared slowly as the condition of the diseased organ improved; the outlines of the hyperalgesia became irregular, until finally there was only a small area of hyperalgesia remaining. After several days it was impossible to state that the area found hypersensitive to pain corresponded to a segmental zone, because it had become so vague.

The zones may disappear after repeated examinations. Thus we have often observed that after the skin of a patient had been examined in succession by a number of the house staff, the zone became less and less distinct, and finally disappeared. After a short interval of rest the hyperalgesic area again appeared. We have always considered that this disappearance of cutaneous hyperalgesia after a number of examinations which followed each other in close succession was a sign that the nerves had become "tired out."<sup>9</sup>

The zones may disappear suddenly in the course of the visceral disease, with persistence or sudden increase in the general symptoms. We have seen this sudden disappearance of skin hyperalgesia in a number of instances, and shall speak of its significance later.

<sup>8</sup> In some cases the hyperalgesia is so intense that the zone can be mapped out in spite of the fact that the skin is more or less anesthetic from the cold. Care, however, must be taken that the cutaneous tenderness due to a bruise or superficial abscess is not confused with referred cutaneous hyperalgesia.

<sup>9</sup> It may be that the relief from pain obtained by the application of cold to the abdomen in acute abdominal disease is due to the anesthesia of the skin produced. On this theory we have, in some acute affections with Head zones, anesthetized the hyperalgesic area with menthol (50 per cent.). In some of the patients the pain was relieved.

#### IV. THE GENERAL SIGNIFICANCE OF LOCALIZED AREAS OF CUTANEOUS HYPERALGESIA IN VISCERAL DISEASE.

While the absence of a characteristic zone of cutaneous hyperalgesia in a suspected affection of an abdominal organ does not mean that there may not be a disease of that organ, the presence of the zone means that there is an undoubted lesion. From this one must not conclude that the viscus which gives the zone is the one which causes the symptoms, for we may get a zone from an organ which is secondarily affected. Thus we have seen, in several patients with marked abdominal distention in the course of typhoid fever, a zone of hyperalgesia of the tenth and eleventh dorsal segment on the right side corresponding to the cecum and vermiform appendix, an evidence of especial distention in those structures.<sup>10</sup>

The presence of a Head zone alone must not be the only factor in arriving at a diagnosis; it must be used in conjunction with other signs and symptoms. Used with circumspection, however, it will be found of value in very many patients.

The signs of not a few abdominal affections are so much alike that the presence of a Head zone may focus attention on one or the other organ, with the probability that the disease will be found in that organ. At any rate, the presence of a zone must focus the clinician's attention upon the corresponding organ, and lead to a more careful examination of the organ and its surroundings. When the symptoms and signs have left us in doubt which of several viscera was the seat of the lesion the presence of a zone corresponding to the one or other viscus has made the diagnosis possible. In not a few patients with marked abdominal distention and rigidity the presence of a characteristic zone has aided very much in making a differential diagnosis between disease of the gall-bladder and of the vermiform appendix, between disease of the gall-bladder and kidney, between disease of the appendix and female adnexa, etc. In early stages of abdominal disease, zones of hyperalgesia are also of value, and have aided us in making an early diagnosis.

There is no constant relation between the severity of the pain or the gravity of the lesion and the degree of sensitiveness of the skin; we have seen very marked zones with little subjective pain and slight lesions, and only slight hyperalgesia in patients with very severe pain and grave lesions.

A few facts must be mentioned concerning the significance in an abdominal affection of the sudden disappearance of a Head zone with the persistence of other symptoms and signs. We have given

<sup>10</sup> After distending the sigmoid flexure with air or fluid by means of a tube introduced into the rectum, one can often find a characteristic zone of hyperalgesia of the tenth and eleventh dorsal segments corresponding to the sigmoid.

especial attention to this point, but have not yet reached any positive conclusion. We do not agree with those who have claimed that the sudden disappearance of a zone means relief of tension in the corresponding viscus. Based on this, some writers have claimed, in acute appendicitis, for example, that with perforation of the appendix the zone should be absent or should suddenly disappear. We have observed a large number of cases of perforative appendicitis with persisting Head zone. (See Affections of the Appendix.)

We have gained the impression, however, that with persisting or increasing symptoms, the sudden disappearance of a zone is a sign of ill-omen and cause for concern. Thus, we have seen several patients with mild symptoms of appendicitis and with a Head zone suddenly develop very severe symptoms, making immediate operative interference imperative. Examination just before the operation showed that the appendix zone had disappeared.

The subject requires further study before any positive statements can be made.

The presence of areas of skin hyperalgesia corresponding to several viscera may mean a combined lesion of several adjoining viscera, although in these patients one has to think of a disease of the spinal cord itself. In this connection the following case is of interest:

A young girl with indefinite abdominal symptoms and with some tenderness in the right iliac region was sent into the hospital with the diagnosis of chronic appendicitis. Examination showed that there was some tenderness in the appendix region and some abdominal rigidity, with fever. There was an extensive area of skin hyperalgesia extending over the right side of the abdomen from Poupart's ligament to above the free costal border. This at once directed attention to the vertebral column and spinal cord. Careful examination revealed a slight scoliosis of the dorsolumbar vertebræ. An injection of tuberculin was followed by a marked general and local reaction; the *x*-rays showed beginning disease of several vertebræ. The patient was suffering from early Pott's disease.

#### V. GENERAL CONSIDERATIONS.

In what follows we shall speak of the zones by the names of the viscera to which they correspond rather than to the spinal segments to which they belong. Thus, we shall speak of gastric, gall-bladder, appendix, kidney zones, etc. Head has demonstrated conclusively the visceral associations of the various hyperalgesic areas; we believe it will add to the clearer understanding of the zones if they are directly named according to the viscera to which they correspond.

We desire to call attention to the fact that the zones of hyper-

algnesia that we have found differ somewhat from the zones described by Head, both in outline and extent. Thus, the stomach zone, according to our experience, corresponds to the seventh, eighth, and ninth segments of Head (according to Head, sixth, seventh, eighth, and ninth); the gall-bladder zone to the eighth and ninth segments on the right side (same as Head's diagrams); the appendix zone, according to our experience, tenth and eleventh segments of Head on the right side. In our diagrams we have drawn the zones as we have found them in our cases. It will be

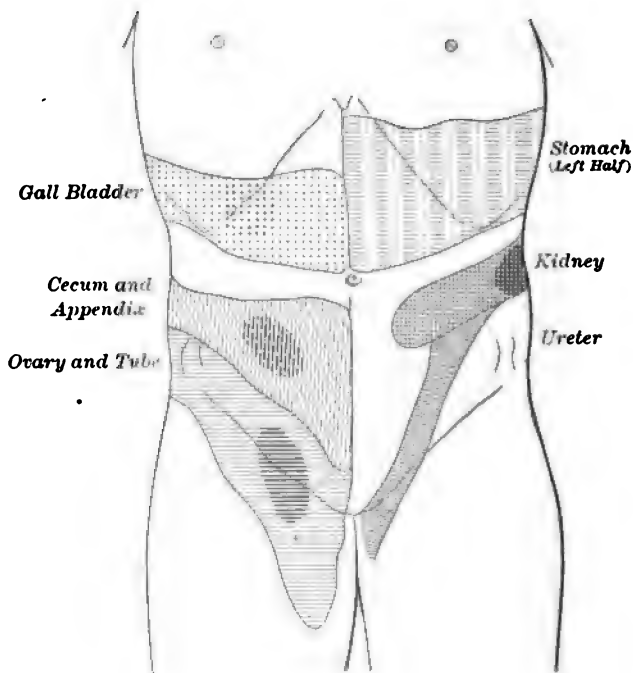


FIG. 1.—The general location and outline of the zones of cutaneous hyperalgesia for some of the abdominal viscera. Anterior view. The maxima are deeply shaded. Only the left half of the gastric zone is given. The ureteral zone consists of a series of maxima (diagrammatic).

found, in the description of the zones, that we do not absolutely limit the posterior portions. Thus, we say, in describing the gastric zone, that it extends from the sixth to the tenth vertebræ, approximately. The zones, except the gastric zone, stop sharply at the posterior median line, but their upper and lower margins are more variable.

The zone appears on that side of the body on which the affected organ has its nervous connections; the side on which the organ is normally situated. If an organ belongs on the left side, the hyper-

algescic zone will be found on that side, even if the organ, through disease or mobility, lies on the other side of the body.

We will call those areas "objective zones" when the patient suffers actual pain as the stroking pin enters them. All less painful zones will be called "subjective zones." By an "anterior zone" we mean an anterior maximal area; by a "posterior zone," a posterior maximal area.

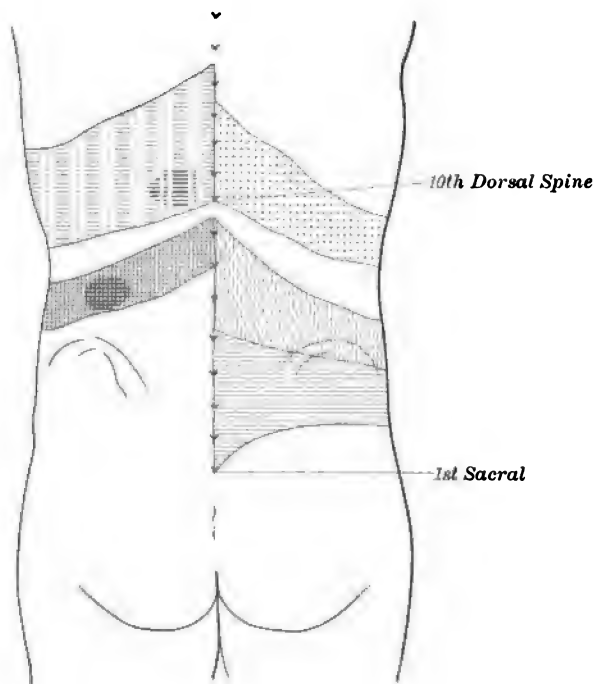


FIG. 2.—The general location and outline of the posterior parts of the zones (diagrammatic).

**THE STOMACH.** We have examined only a small number of patients with gastric affections, and have found the zones more variable in extent and configuration than in any of the other abdominal diseases. Head, in his original paper, stated that the gastric zones appeared most often on the right side. We have found that a complete gastric zone is uncommon. It extends as a broad belt all around the body. In the median line in front it extends from the xiphoid almost to the navel; it then passes upward and backward on both sides toward the spine, where it extends from the sixth to the tenth vertebra (approximately). Incomplete zones are more frequent, either an anterior portion extending to the right or to the left, or on both sides of the anterior median line. Zones were present in some of our cases of chronic gastric diseases with pain

(carcinoma, benign stenosis of the pylorus, chronic bleeding ulcer); more often in acute gastric affections (ulcer, acute dilatation, gastritis). We present a few illustrative cases:

*Acute Bleeding Ulcer.* There was a well-marked gastric zone in its left half, while the bleeding was going on; when bleeding and pain ceased, the zone disappeared simultaneously.

*Benign stenosis of the pylorus* in a patient who vomited once a day, at which time he had considerable pain and tenderness. Several times, after the vomiting, a complete gastric zone could be mapped out; at other times, only the anterior half on the zone was present.

*Benign Stenosis of the Pylorus; Cholelithiasis.* Five years' history of cholecystitis. During the last six months, occasional vomiting and frequent eructations not associated with attacks of cholecystitis. There were dull pain and moderate tenderness in the right hypochondrium; frequent nausea and eructations; vomiting. There was a complete gall-bladder zone extending to the left as far as the anterior axillary line, a narrow strip of hyperalgesia corresponding to a section of the gastric zone. At the operation there was found a small gall-bladder contracted about numerous stones and dense pericholecystitic adhesions which kinked the pylorus to an acute angle.

In visible gastric peristalsis from various causes, we have at times observed the anterior part of the gastric zone appear, and disappear when the peristalsis ceased. We have not found gastric zones in patients who had gastric symptoms (nausea and vomiting) in the course of acute abdominal affections, such as appendicitis, cholecystitis, etc., but the zones corresponding to the diseased viscera were present. In this connection the zones have sometimes been of diagnostic value, as in the case of a female, aged fifty years, who was admitted to the hospital on account of repeated vomiting, with generalized abdominal pain and tenderness. The search for skin hyperalgesia revealed not a gastric zone, but one for the uterus and adnexa. The lesion proved to be a retroflexed uterus with diseased adnexa, and the vomiting was reflex.

Before leaving the subject of gastric zones, we desire to add a remark on the subject of the so-called tender point in gastric ulcer that is often found on the back opposite the tenth dorsal vertebra. Many patients point to this as the region of greatest pain. This tender point will be found to lie within the area of gastric hyperalgesia, and to correspond to the posterior maximum of the gastric zone. This fact may be the explanation of the tenderness and pain experienced in this region by many patients with gastric ulcer.

**THE DUODENUM.** The duodenal zone lies between the gall-bladder and the appendix zones. It lies almost completely to the right, but in two of the patients extended slightly to the left of the anterior median line. Anteriorly it is broad; its upper limit is

about on a horizontal line midway between the umbilicus and the ensiform cartilage; its lower border is a little below the umbilicus. It extends backward and slightly upward, and narrows; at the anterior axillary line it is very narrow (about  $1\frac{1}{2}$  inches); it then becomes broader, and is lost about the midscapular line. It corresponded roughly to the ninth right dorsal zone of Head in the few patients we have examined.

No.	Disease.	Symptoms.	Zone.
1.	Perforated ulcer.	Fever, acute abdominal symptoms.	Well-defined.
2.	Bleeding ulcer.	Melena, colic, slight tenderness.	Well-defined.
3.	Bleeding ulcer.	Melena, colic, slight tenderness.	Well-defined.
4.	Bleeding ulcer (chronic).	Slight pain and tenderness.	Absent.

The diagnostic significance of Head's zones was well illustrated in Case 1:

*Perforated Duodenal Ulcer, with Hyperalgesic Zone Corresponding to the Duodenum.* The patient entered the hospital with a three days' history of abdominal cramps, which became localized in the right half of the abdomen; at the onset he vomited and was constipated. A similar attack four weeks before had been treated as appendicitis. On admission, temperature,  $101^{\circ}$ ; pulse, 100. General condition fair; slight rigidity of right rectus muscle; moderate tenderness a little below and to the right of the umbilicus. The patient was supposed to have a mild appendicitis. There was indistinct hyperalgesia on the right side above the navel. The following day the temperature was normal, and the patient complained of cramps in the right lower abdomen. Physical signs unchanged, except that a well-marked duodenal zone was now present. Although the zone of hyperalgesia was recognized as duodenal, the diagnosis of appendicitis was adhered to. The operation, on the following day, revealed a small perforation of the duodenum from an ulcer in its descending portion with numerous adhesions around it.

**GALL-BLADDER AND LIVER.** According to our experience, a zone is present in acute affections of the gall-bladder more often than in any other acute intra-abdominal affection. In these cases the Head zone has often been a valuable diagnostic aid. In many cases an enlarged, tender, and palpable gall-bladder makes the diagnosis easy, but the recognition of the disease is often difficult or impossible in stout patients without jaundice, with marked abdominal distention and rigidity. These patients may refer their pain to the right lower abdomen, and may have their tenderness in this region. Acute intestinal obstruction, acute pancreatitis, or acute appendicitis are diagnoses often made. In some patients the presence of a zone of hyperalgesia has been the only localizing sign.

The gall-bladder zone lies in the right half of the abdomen, above the level of the umbilicus. The complete zone starts exactly at the median line in front, extending from some distance below the

xiphoid to a short distance above the navel. Tracing it backward, it slants obliquely upward and becomes narrow, passing partly over and partly below the costal arch. It is narrowest at the midaxillary line, where it is about two inches wide. Posteriorly it becomes broader, and at the spines it is about as wide as in front. In some cases, more or less of the anterior portion only has been present (maximal area).

In 21 cases of acute cholecystitis a zone was present eighteen times. The complete zone was present eleven times, the anterior part alone eight times. The zone was present four times in 5 cases of gangrenous cholecystitis; it was found in all 3 cases of empyema, and in both cases of acute cholecystitis with seropurulent peritonitis that were examined.

In the following illustrative cases the zone was an important diagnostic aid:

*Acute Cholecystitis and Cholelithiasis; Diagnosis impossible on Account of Delirium.* Female, aged seventy years, admitted with a three days' history of general abdominal cramps, never localized; vomiting and fever. On admission the patient was very delirious; the abdomen was everywhere rigid, and seemed to be everywhere tender. Temperature, 105.4°. There was a marked objective anterior zone for the gall-bladder, and this was the only means of locating the lesion. The operation was done under local anesthesia, and revealed acute cholecystitis with pericholecystic abscess, due to calculi. If general anesthesia had been employed, palpation of the enlarged gall-bladder might have been possible, but because of the patient's poor condition, local anesthesia was used.

*Acute Gangrenous Cholecystitis Presenting the Symptoms of Acute Intestinal Obstruction.* Female, aged forty years, with four days' history of severe epigastric cramps, persistent vomiting, absolute constipation. Enemas ineffectual. Under observation, patient vomited feculent material. The abdomen was markedly distended, rigid, and very tender in its entire upper half. No mass. Complete gall-bladder zone. Acute gangrenous cholecystitis was found at operation.

In a second case, similar to this one, there was a marked anterior zone. A third case, however, with similar symptoms, had no zone.

*Acute Gangrenous Cholecystitis with Reflex Anuria in a Patient with Old Renal Disease, Simulating Pyonephrosis.* In a male, aged forty-three years, there was a two years' history of a right kidney disease, with occasional attacks of renal colic and pyuria; four days before admission severe pain in the right upper abdomen, vomiting, and diminution of urine. These symptoms persisted, the pain radiating to the right flank, the vomiting frequent, and the urine scanty and turbid. On admission, moderate tenderness in the entire right upper quadrant of the abdomen, marked rigidity of



the right rectus, especially in its upper half; no mass. Neither kidney palpable, but palpation for the right kidney very painful. Temperature, 103°. Urine slight in amount (7 ounces in twenty-four hours), full of pus, albumin, and casts. Moderate oedema over both tibiae. There was a marked complete zone for the gall-bladder. The clinical diagnosis was pyonephrosis with partial reflex anuria. The day after admission, however, the rigidity had partly disappeared and an enlarged, very tender gall-bladder was palpable. The zone persisted. Temperature remained high, and the patient was operated on and an almost completely gangrenous gall-bladder was found. The infection from the cholecystitis had probably interfered with the function of the kidneys, one of which was seriously damaged. This view was borne out by the post-operative course; after a few days the patient passed much larger quantities of urine.

In the less acute affections of the gall-bladder the zone is often present, but is not of such diagnostic value, because there is less rigidity of the abdomen and more localization of the symptoms. However, we have seen a number of patients at the end of an attack, or after an attack, in whom the presence of the zone has materially helped us to make the diagnosis. The following is an example:

*Calculus in the Cystic Duct, with a History of Attacks Diagnosed as Appendicitis.* A boy, aged twenty years, was admitted to the hospital with the history of an attack of right iliac pain and vomiting two years before. His present attack began four days before admission, with severe non-radiating pain in the right lower abdomen. No vomiting, no urinary symptoms, no jaundice. Twenty-four hours before admission the pain had subsided, and at the time of admission there was no pain. The physical examination was negative. There was a moderately developed anterior zone for the gall-bladder, of typical shape. Previous attacks had been diagnosed as appendicitis. At the operation the appendix was normal; the gall-bladder was small, contained a large stone lodged in its neck, with numerous pericholecystic adhesions.

In chronic cholecystitis due to cholelithiasis, zones are often present; although diagnosis without them is usually easy from the characteristic history. Some of the cases, however, present a history that is purely gastric, and, if a zone is present, it may aid in the differential diagnosis. We have examined 19 cases of chronic cholecystitis and cholelithiasis that entered the hospital with histories of previous attacks; 11 of these had zones, mostly of the incomplete anterior variety.

An illustrative case with a gastric history:

*Chronic Cholecystitis, with Vomiting and Epigastric Distress.* Female, aged thirty-eight years, had for two years frequent attacks of nausea and eructations after eating, and occasionally vomiting. There was constant dull pain in the epigastrium. On two occasions

there were sharp sticking, non-radiating epigastric pains. The physical examination and gastric findings were negative. At the first examination there was no zone. On the fourth day of observation the patient "ate something that did not agree with her," and had more epigastric pain than usual; there was now present an anterior, moderately developed gall-bladder zone. The operative finding was a markedly thickened gall-bladder, with adhesions that stretched to the duodenum, and several large calculi.

In pancreatic disease with dilated gall-bladder a zone for the gall-bladder is sometimes present. We have seen 5 cases of carcinoma of the head of the pancreas with dilated gall-bladder, in 2 of which an anterior gall-bladder zone was present. Two cases of chronic pancreatitis with distended gall-bladders were seen; both had anterior gall-bladder zones. We do not know if pancreatic zones exist. In several cases of acute and subacute pancreatitis that we have studied there was no skin hyperalgesia. In abscess of the liver, in acute congestion of the liver (from cardiac disease, etc.), and in cirrhosis of the liver, we have found in some of the cases hyperalgesia over the lower right chest. The areas of hyperalgesia were very irregular, and corresponded to no zone.

**KIDNEY AND URETER.** The kidney zone is wide at the posterior median line, where it begins, and gradually narrows anteriorly. Its greatest breadth is at the spinal column. It narrows to make a triangular area, with a rounded apex, situated a little to that side of the anterior median line on which the zone lies. We have never seen the kidney zone quite reach the anterior median line. Each zone is strictly limited to its half of the body. There is no difference in contour between the right and left kidney zones. The kidney zones are complicated by the additional ureteral zones that are present in certain cases. The ureteral zone springs, so to speak, from the lower margin of the kidney zone at the anterior axillary line. In an average adult it is about three inches wide at this beginning. It narrows in its downward course, and passing obliquely downward and forward, it terminates on its side of the penis and scrotum in the male; the labia in the female. After the first narrowing it widens again well below the umbilical level. In the male, after this swell, it can be ascertained that the zone spreads fan-shape to the anterior median line over the pubic area and its half of the scrotal and penile skin. There are anterior and posterior kidney maximal areas. The ureteral zone seems to be made up of a series of maxima. The kidney and ureteral zone is most often present, as in the other intra-abdominal affections, in the presence of pain and tenderness.

We have examined 14 patients with renal calculus, and have found a more or less marked zone six times. In most of the cases in which the symptoms were slight no hyperalgesia could be demonstrated. Two of four cases of pyelitis had zones, as had one patient

with an acute pyelonephritis; one of infected hydronephrosis due to calculi, one of septic infarct in acute endocarditis, one of pyonephrosis. The more acute the renal affection, the more apt is there to be a cutaneous hyperalgesia. Thus we have not found a zone in the large majority of patients with tumors of the kidney, with the exception of one case, in which the operation showed that there was a large fresh hemorrhage into the tumor.

When a calculus passes into the ureter from the kidney, the kidney zone is apt to disappear and a ureteral zone develop. We have observed this in several instances, and have been able to follow the passage of the calculus along the ureter by means of the skin hyperalgesia. Of 8 cases of stone in the ureter, there was a more or less well-marked zone in 6. In a case of rupture of the kidney, there developed a well-marked ureteral zone after a severe colic. The colic and zone disappeared after the passage of a blood clot. The diagnostic value of localized areas of skin hyperalgesia in kidney and ureteral affections is not as great as in other abdominal affections, but in some patients it has had practical usefulness. In one case the findings were of considerable interest:

*Calculous Anuria; Left-sided Pain; Right-sided Zone.* A man was admitted to the hospital with a three days' history of pain in the left flank and almost complete anuria. On admission he was drowsy, and did not complain of pain. There was a marked objective zone for the right kidney. At operation there was found a double calculous pyonephrosis; the left kidney was atrophic and did not contain any urine; the right kidney was less diseased, was the seat of recent inflammation, and contained some urine.

Experience may show that in cases of this kind the zone may help in determining which kidney should be operated upon.

The presence of a ureteral zone on the right side has helped us to distinguish ureteral calculus from appendicitis in several cases, but our experience has been too small for any positive statements as to its value. We believe that the absence of a ureteral zone and the presence of an appendix zone make the diagnosis of a ureteral calculus at least doubtful, even though there are well marked urinary symptoms. On the other hand, the presence of a ureteral zone must make one suspect trouble in the ureter, in spite of absence of urinary symptoms. In this connection the following case is of interest:

*Suspected Ureteral Calculus on Account of Suspicious X-ray Shadow and Red Blood Cells in the Urine; Well-marked Appendix Zone; Appendix Found Diseased.* A man, aged forty-four years, gave a history of sharp pain in the right lower abdomen for three days. On admission there was tenderness in the right iliac fossa, slight rigidity of the rectus, temperature, 101°. There was a moderately developed anterior zone for the appendix. The urine contained a few casts and pus cells. During the four succeeding days

there was pain at times. The zone disappeared in two days. After cystoscopy and ureteral catheterization, there were a few red blood cells in the urine. X-ray showed a "suspicious shadow" in the lower part of the right ureter. The ureter was exposed by the extraperitoneal route, and was found empty. The peritoneal cavity was opened, and a very adherent, acutely inflamed appendix was removed.

**VERMIFORM APPENDIX.** The zone begins at the median line in front, sometimes a little to its left, from a point a short distance below the umbilicus to one equally distant from the symphysis pubis. It narrows toward the anterior axillary line to a width of about two inches (average adult). From this line it widens and spreads to the posterior median line from the eleventh dorsal to the second lumbar spines (approximately). At the anterior median line there is often a tongue-like downward extension of the zone (see diagram). There is an anterior maximal area which is sometimes present alone. We have not seen posterior maxima. It may be that the "appendix" zone is really an "appendix and cecum" zone, because the cecum is so frequently involved in appendicitis. Sometimes, when an ice-bag has been employed over the appendix region, only the posterior half of the zone is present.

Diagnosis has been aided in a considerable number of the patients by the presence of the zone, especially in that large class of acute cases in which the abdomen is rigid and there is no palpable mass. The zone has been of the greatest value in helping to differentiate between diseases of the appendix, on the one hand, and those of the gall-bladder or right uterine adnexa, on the other.

We have already stated that the absence of a zone is of no significance. But if a patient complains of symptoms which resemble appendicitis, and a zone is not present in the right lower abdomen, it is well to look elsewhere for hyperalgesia. Thus, we have seen several cases of beginning pneumonia that had considerable pain, tenderness, and rigidity in the right iliac region, in which hyperalgesia over the thorax first led to careful examination of the lungs.

Careful examinations in a large number of cases of acute and chronic appendicitis have given the following results: In the majority of cases of chronic appendicitis, or, more properly, cases of appendicitis admitted for operation in the interval, we have found no zone. In some patients, who entered the hospital with the history of a recent attack, a zone of hyperalgesia could be demonstrated. We tabulate the acute cases:

	Cases.	Zone present.	No zone.
Acute appendicitis . . . . .	20	14	6
Acute appendicitis with peritonitis . . . . .	21	17	4
Acute appendicitis with abscess . . . . .	35	21	14
Acute appendicitis with abscess and peritonitis . . . . .	15	12	3
Acute appendicitis, gangrenous and perforating . . . . .	15	13	2
Empyema . . . . .	8	5	3
Total . . . . .	114	82	32

Thus, in over 70 per cent. of the patients with acute appendicitis the characteristic hyperalgesic zone was present. It was complete, extending from the median line in front to the median line behind, and with characteristic outline in the greater number of the cases. In more than 50 per cent. of the patients with an abscess and a history of more than six days' duration the zone was absent. If these cases are excepted, the "appendix zone" was present in almost 80 per cent. of patients with recent acute appendicitis.

In the following are given short histories of some cases of special interest:

*Acute Appendicitis (Retrocecal).* Three days' history of severe pain in the right upper abdomen, radiating to the right flank, one chill, and fever. Rigidity of the whole right rectus. Marked tenderness at two points: one in the right hypochondrium in the axillary line, the other at McBurney's point. Markedly developed anterior appendix zone. The appendix found adherent to the anterior surface of the kidney.

*Acute Appendicitis, with Jaundice.* Five days' history of severe cramps in the right half of the abdomen, that localized a little below the umbilical level. The right rectus was equally rigid above and below. No mass. Moderate fresh icterus of the skin and conjunctivæ. Markedly developed anterior appendix zone. At operation, liver and gall-bladder were normal. The jaundice was due either to toxemia or to gastroduodenitis.

*Acute Appendicitis, with Appendix Zone and Zone for the Right Adnexa, which were Secondarily Inflamed.* On admission there was a twenty-four hour history of pain in right lower abdomen, and vomiting. There was no fever. Moderate tenderness over McBurney's point. No zone. The next day, the symptoms persisting, there was a markedly developed complete appendix zone. That evening a zone for the right uterine adnexa developed in addition to the appendix zone. At operation the appendix overlay the right tube, which was acutely congested. Two days after operation the zone for the right adnexa, which began to fade twenty-four hours after operation, was gone.

*Acute Gangrenous Appendicitis; Chronic Pyosalpinx.* After a puerperal infection two years ago there had been pain in the right lower abdomen, radiating down the thigh, leukorrhœa, and dysmenorrhœa. Occasional exacerbations of the pain, with chilly sensations and fever. Three days before admission there was an attack of severe pain in the right lower abdomen, and vomiting. Marked tenderness in the right iliac fossa and marked rigidity of the right lower rectus. No mass felt through the abdomen. By vagina there was an elastic, slightly tender mass in the right vaginal vault. Moderately developed complete appendix zone. At operation, in addition to the appendix lesion, there was an old adherent pyosalpinx.

*Acute Appendicitis in the Puerperium.* Six weeks before admission patient was delivered of a child. During the puerperium there was fever and pain in the right lower abdomen. After the two weeks' puerperium pain in the right lower abdomen continued. Three days before admission pain became more marked, cramp-like, and accompanied by fever. There was marked tenderness and rigidity of the right lower abdomen. Marked tenderness in the right vaginal vault. Moderately developed complete appendix zone.

*Acute Appendicitis; General Purulent Peritonitis.* Symptoms began four days before admission, with general cramps that never localized, and vomiting. The patient entered the hospital in a moribund condition, with the signs and symptoms of an advanced peritonitis without any focal signs. There was a moderately developed anterior appendix zone. Patient was not operated on; the postmortem showed the lesion.

In the general discussion of hyperalgesic zones attention was called to the significance of *sudden appearance and disappearance of zones*, with persisting symptoms. We summarize here our experience in appendicitis:

*Gangrene of the Mesenterium of the Appendix.* For four days there had been slight pain in the right lower abdomen. On admission temperature and pulse were normal; there was no pain, and only very slight tenderness in the right iliac region. There was a markedly developed complete appendix zone. The next day chill; temperature, 104.2°; abdominal signs unchanged. The zone had disappeared. Immediate operation disclosed an acutely inflamed appendix, with complete thrombosis and gangrene of the mesenterium.

*Ruptured Appendiceal Abscess.* Patient entered the hospital with a small, very tender mass in the appendix region. There was a moderately developed anterior appendix zone. Patient complained of slight cramps in the right lower abdomen. Two hours after admission the cramps had ceased, but the patient looked much worse, and the whole abdomen was rigid. The zone had disappeared. At the operation, the abscess was found discharging pus into the general peritoneal cavity.

*Ruptured Appendiceal Abscess.* On admission, patient complained of slight pain in the right lower abdomen, where there was an egg-sized, very tender mass. There was a markedly developed complete appendix zone. One-half hour later cramps became generalized, and the abdomen was rigid, and there was only a slightly developed irregular appendix zone. Findings at operation as in the former case.

*Ruptured Appendiceal Abscess.* On admission, an orange-sized mass, with slight rigidity of the lower right rectus. Patient complained of very slight pain. There was no zone. Three hours later there was more pain of crampy character; otherwise the symp-

toms and signs were unchanged. A moderately developed anterior appendix zone had appeared. At operation the abscess was leaking pus at one point into the general peritoneal cavity.

*Appendicitis in Typhoid Fever.* We have seen four cases of acute ulcerative and one case of subacute appendicitis that developed in the course of typhoid. All of them except one of the acute ulcerative cases had well defined appendix zones. All of the cases had pain and tenderness. In one of them the nature of the zone helped in differentiating from typhoid perforation.

**INTESTINES.** Irregular areas of hyperalgesia were present in some of the cases of intestinal tumors and of intestinal obstruction that we have studied, but they have no uniform shape and do not seem to be of any value. The only intestinal lesions in which there was uniformity in the zones were ileocecal tuberculosis and perforation of the ileum.

*Ileocecal Tuberculosis.* The zone that we have seen in these cases was a large area of hyperalgesia occupying the whole right lower abdomen down to Poupart's ligament, often extending a little to the left of the median line, and posteriorly becoming lost about the posterior axillary line. In nine cases the zone was present five times. In one case with abscess formation and a three weeks' history, the zone was the only finding that militated against the diagnosis of appendicitis abscess. In another case, with vague pain and melena, the zone gave the first suggestion that the lesion—induration of the ileocecum and adhesions—was in the right lower abdomen.

*Perforations of the Ileum.* In several cases of free typhoid perforations of the ileum a zone was not present. All the patients were delirious, and at operation there were gas and feces in the general peritoneal cavity. We saw two slow typhoid perforations, both presenting marked zones; their histories are very much alike, and we give one:

During the whole third week of the disease the patient complained of colicky pain in the right lower abdomen, which on the day of admission (twenty-third day of illness) had become more marked. The patient was delirious. The whole abdomen was rigid. Exceedingly marked objective zone, resembling the zone in ileocecal tuberculosis, but extending more to the left of the median line. At operation the lower ileum was adherent and feces were present only in the pelvis.

We saw only one case of perforated tuberculous ulcer of the lower ileum that presented a history like appendicitis, and in which the only finding against appendicitis was a zone like that of the slow typhoid perforations. This, too, was a slow perforation, the loop of gut involved being found wrapped in omentum.

**UTERUS AND ADNEXA.** Head describes differences between the zones for the uterus, the ovary, and the tube, which we have been

unable to verify. The zone for the right adnexa lies on the right half of the median line; that of the left adnexa on the left half; the zone for the uterus is a combination of the two.<sup>11</sup> There is no difference between the zones for the right and left adnexa. Beginning some distance above Poupart's ligament, the upper margin of the zone runs parallel to it, and pursues this obliquely upward course to the spine of the second lumbar vertebra (approximately). The lower margin is a long, tongue-like process that extends half-way down the thigh on its inner aspect. The lower margin, as it passes a short distance below the anterior superior spine of the ileum, approaches the upper, the average breadth of the zone here being three inches. The lower border then passes horizontally backward over the buttock to reach the posterior median line partly over the sacrum. Sometimes the upper half of this zone is better developed, sometimes the lower; these may be considered maxima.

Diagnosis in the diseases of the uterus has not been aided by the presence of a zone, and we will therefore dispose of this heading briefly. In about half of the cases of dysmenorrhœa and of endometritis with pain the zone was present. Some of the cases of retroflexion, retroversion, antelexion, and prolapse showed the zone. It was present in the five cases of uterine polyp that we observed (all of them had pain). It was not present in tumors of the uterus, except in a few cases.

In diseases of the tubes and ovaries, especially those of the right side, the zones have been of diagnostic value.

	No. of cases.	Zones present.
Pyosalpinx, acute . . . . .	9	9
Pyosalpinx, acute, double . . . . .	3	2
Salpingo-oöphoritis . . . . .	7	4
Salpingo-oöphoritis, double . . . . .	5	4
Ovarian abscess . . . . .	3	2
Ovarian cyst, twisted . . . . .	3	3
Ectopic gestation . . . . .	9	5
Total . . . . .	39	29

A large number of cases that presented few or no symptoms have not been included in the above list, because the majority had no zones. There were no zones in a large number of patients with tumors and cysts of the ovary.

We present some illustrative cases in which the presence of the zone aided diagnosis:

*Bilateral Acute Suppurative Salpingitis; Seropurulent Peritonitis.* Physical signs of appendicitis, with a small mass low down in the right iliac region. Marked zone for the right, less marked zone for the left adnexa. At operation, the right tube showed the

<sup>11</sup> It is very difficult to determine a separate zone for the uterus, because in so many cases in which the uterus is diseased the adnexa, too, are diseased.



more marked lesion, the palpable mass being made of omentum that enwrapped it.

*Right Suppurative Salpingitis; Diffuse Purulent Peritonitis.* The patient, aged fifty-five years, entered the hospital in a delirious condition. Her history indicated appendicitis. The abd men presented the signs of a generalized peritonitis; no focal signs. There was a marked zone for the right adnexa.<sup>12</sup>

*Right Pyosalpinx; Streptococcic Peritonitis.* Abdomen rigid and tender throughout. History suggested perforated gastric ulcer. Marked zone for right adnexa, slight zone for left adnexa. Vaginal examination negative. At operation the left tube was deeply congested; contained streptococci. Pus from right tube showed streptococci.

*Left Twisted Ovarian Cyst Lying on the Right Side.* Three days' history in a patient, aged seventeen years, suggesting appendicitis. Marked tenderness and slight rigidity of the right lower abdomen. Tenderness and fulness on the right side by rectum. Marked zone for the left adnexa. At operation the cyst, springing from a long pedicle, lay behind the right uterine adnexa. The correct diagnosis in this case was suggested by the Head zone alone.

## VII. CONCLUSIONS.

1. We agree in the main with the statements of Head, that there are present, in many affections of the abdominal viscera, constant and definite areas or zones or cutaneous hyperalgesia.

2. These zones may vary somewhat in extent and in outline, but they have a characteristic location.

3. The presence of a characteristic zone is an evidence of an affection of the corresponding abdominal viscus, although not of necessity the affection which is causing the symptoms.

4. The zones are present in a large percentage of patients with acute affections of the appendix, of the gall-bladder, of the uterine adnexa, and are of considerable value in the diagnosis of these acute affections.

5. Zones are frequently present in acute disease of the other abdominal viscera, and when present aid in making the correct diagnosis.

6. Cutaneous hyperalgesia may appear early in acute abdominal disease. Its presence is no index of the gravity of the lesion. Its sudden disappearance may be of grave significance.

<sup>12</sup> At the postmortem examination there were streptococci in the small amount of pus in the right tube. Cultures from the vagina and from the uterus showed streptococcus. Cultures from the left tube, which contained no pus, were sterile. In the left horn of the uterus was a polyp that completely blocked the uterine opening of the left tube. The case was evidently one of ascending infection. The findings account for the absence of a zone for the left adnexa.

7. In the absence of all other localizing signs or symptoms, the zone may indicate the organ that is affected. In most instances, however, it must not be used to make the diagnosis, but only as a diagnostic aid, to substantiate conclusions reached from a consideration of all the symptoms and signs.

## TUMOR OF THE GASSERIAN GANGLION.<sup>1</sup>

A REPORT OF TWO CASES, WITH NECROPSY.

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TUMOR arising in the Gasserian ganglion or having its chief clinical manifestations in disturbance of this ganglion is fortunately rather rare, but doubtless far more common than is generally believed. Brain tumor is always serious in its symptomatology, but when the Gasserian ganglion is implicated the pain is usually intense. The first case of tumor in this region recorded in this country, and the second case on record in which operation was performed, is that reported by Dercum, Keen, and Spiller (1900). Since then two cases with necropsy, in one of which operation was done, have come under my care.

CASE I.—A K., aged twenty-five years, was referred to the University Hospital by Dr. H. S. Crouse, of Littlestown, Pa., March 4, 1907. Dr. Crouse stated that the patient first had paralysis of the right fifth nerve, with severe pain; the right optic nerve was then implicated causing blindness in the right eye, later the left optic nerve became affected causing complete blindness. Then the left arm became paretic. At times the mentality was much impaired, but only when the pain in the head was severe.

The history as obtained after the patient entered the hospital is as follows:

*Chief Complaints.* Blindness, intense headache, vomiting.

*Social History.* Patient is a brick layer and stone mason. He is unmarried. He uses beer and whiskey, sometimes to excess. He chews tobacco rather freely. He had gonorrhœa about a year ago, but has no history of syphilitic infection.

*Family History.* Father and mother are living. Two brothers and three sisters are living and well; one sister died of eclampsia.

<sup>1</sup> Read by invitation at a meeting of the St. Louis Surgical Society, May 29, 1908.

The patient says the members of his family are all more or less "nervous." No family history is obtained of tuberculosis, malignant, cardiac, or renal disease.

*Previous Medical History.* Is negative except that he has had a number of attacks of tonsillitis.

*Present Illness.* The patient is in an advanced stage of mental hebetude, probably as a result of bromism, and his statements are vague and unsatisfactory. He says that last winter he began to have weakness and soreness about the articulation of his jaw (whether the right or left side is not stated), the soreness afterward spreading to his head where it has persisted ever since. About two months ago blindness developed in the right eye and this was followed about two weeks later by blindness in the left eye. During this same period he has vomited a number of times. He is not able to walk unless some one leads him. He believes this inability to walk is caused by his blindness. His general health has not suffered much. Headaches of late have been very severe.

*Physical Examination.* A rather poorly developed and emaciated male subject, looking considerably older than his given age of twenty-five years. Skin is covered with a profuse, deeply colored, red eruption, probably the result of bromides. He has no noteworthy glandular enlargement. Pulse is regular, volume fair. Chest is poorly developed; expansion is fair and equal on both sides. Heart and lungs negative. Abdomen soft and symmetrical. Abdominal organs negative.

*March 6, 1907.* Examination by Dr. Spiller. The left pupil is much larger than the right. Both irides are immobile to light; slight contraction is obtained of each pupil in attempt at convergence. He says he sees light with each eye separately. He wrinkles the forehead well, closes the eyelids, shows the teeth, and draws up each corner of the mouth well, therefore he has no involvement of either facial nerve. Tactile sensation is completely lost in the entire distribution of the right fifth nerve, provided no pressure is produced. Sensation of pain is lost in the same distribution. Sensation is preserved along the border of the lower jaw in the distribution of the cervical nerves. The conjunctiva and cornea are anesthetic in the right eye but not in the left eye. A piece of paper put far up the right nostril is not felt unless pressure is produced, and causes no lachrymal reflex. The jaw goes distinctly to the right when the mouth is opened. The right tonsil is swollen and the uvula is absent. Sensation of the left nostril is normal.

He is distinctly deaf to the voice in both ears. The soft palate moves very imperfectly on the right side. The sense of smell is greatly impaired on each side. The tongue is protruded straight. Taste for salt and sugar probably is lost on the front and anterior part of the tongue. This may have been only on the right side. The grasp of each hand is fair. The upper limbs move freely in

all parts; biceps and triceps tendon reflexes are not distinct on either side. Sensations of touch and pain are normal in each upper limb. Movements in the lower limbs are free in all parts. Patellar tendon reflex and Achilles tendon reflex are lost on each side. Babinski's reflex is not obtained; the toes are not moved distinctly in either direction. Sensations of touch and pain are normal in each lower limb. The gait and station of the patient are very ataxic; he has marked sway with the feet close together.

Examination by Dr. de Schweinitz. Palpebral fissures are equal in width. Left eye is slightly divergent. Movement of the left external rectus is preserved. Movements of internal, superior, and inferior recti are markedly limited. No wheel movement is obtained.

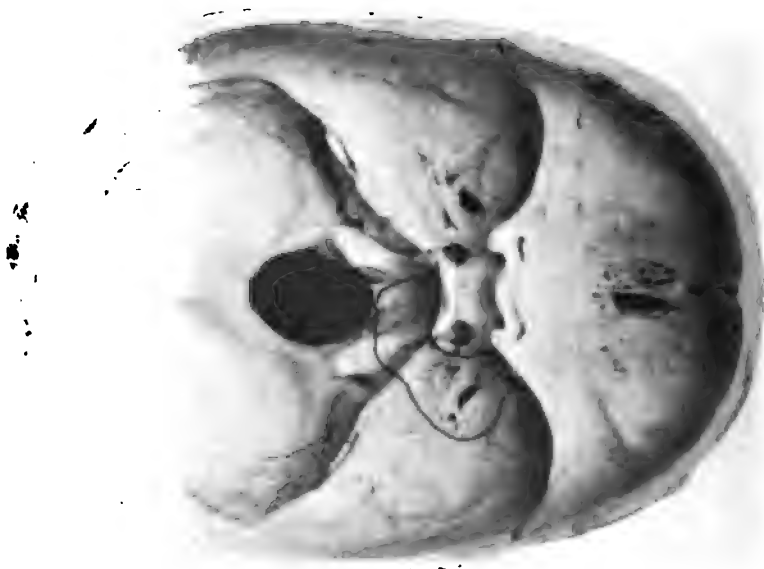


FIG. 1.—Diagram showing the position of the tumor in Case I.

There is loss of movement of the external rectus of the right eye and marked limitation of movements of the superior and inferior recti, with almost lost internal rectus movement. Extensive double optic neuritis is found with large retinal hemorrhages on the right side.

*April 11.* Last night the patient became unconscious; for the last few days he has not seemed to be quite so well. He was transferred to Dr. Frazier's service for operation. A lumbar puncture was made and the cerebrospinal pressure was found to be equal to 27 mm. of mercury (351 mm. of water), and about 15 c.c. of spinal fluid was removed until the pressure was down to 5 mm. of mercury (65 mm. of water).

A decompressive operation was done on each side of the head by

Dr. Frazier just above the ear, in order to relieve the intracranial pressure. The brain bulged much on the right side. The patient died April 12, about 2 P.M.

The brain was removed by me. The right temporal lobe was soft and tightly adherent to the floor of the middle cerebral fossa, and was loosened with much difficulty. A tumor was seen holding the base of this temporal lobe to the dura, and the lobe was removed by cutting through the tumor. The latter seemed to grow from the dura, was most developed at the seat of the right Gasserian ganglion, and nothing was seen of this ganglion, as its position was occupied by the tumor. The tumor covered the floor of the middle fossa in the region of the middle lacerated foramen, foramen ovale, fora-



FIG. 2.—Photograph of the brain removed in Case I. The right temporal lobe is invaded by the tumor. A small tumor of nervous tissue containing nerve cells and medullated nerve fibers is seen on the right side of the cerebellum at the exit of the seventh nerve.

men rotundum as far forward at the right sphenoidal fissure, also the inner part of the petrous portion of the temporal bone in the posterior fossa internal to the internal auditory meatus, and extended over the basilar process as a flat growth as far as the left posterior clinoid process. A round tumor was found invading the base of the right temporal lobe (as described above), and was detached from the lobe in removing the brain, as the lobe was soft. The tumor was firm and measured about 4 cm. in each direction, and extended about 3 cm. into the brain. The right fifth nerve was enveloped in the tumor at its entrance into the pons, and the right third, fourth, and sixth nerves also were caught in the tumor. The tumor did not seem to extend quite far enough to the left to catch the left

third nerve, but came very close to it. It must, however, from the symptoms, have involved this nerve. The bone of the skull did not seem to be implicated. A small hard mass was found at the under part of the right cerebellar hemisphere. The tumor was flat and thin except in the middle cranial fossa.

*Microscopic Examination.* The tumor does not extend into the base of the brain except very slightly at the side of the pons. It covers the pons exactly at the entrance of the fifth nerve into the pons, so that the fibers of this nerve become a part of the tumor immediately beneath the pons. The nerve is completely degenerated at its entrance, as stained by the Weigert hematoxylin method, but the Marchi stain shows numerous fibers in the process of degeneration of the myelin sheaths. The pyramidal tracts are not degenerated. The cells of the motor nucleus of the right fifth nerve are swollen and have peripherally placed nuclei. The sensory nucleus stands out prominently by its yellow color in the Weigert stain, owing to the paucity of medullated nerve fibers; its cells appear somewhat shrunken and some have peripheral nuclei. A considerable mononuclear cellular infiltration is seen about some of the vessels of the pons. These may be cells from the tumor, but they appear somewhat smaller. The fibers of the motor root within the pons show partial recent degeneration by the Marchi method. The pia over the pons presents a distinct round-cell infiltration, suggesting the possibility of syphilis; the pia over the optic chiasm also shows slight round-cell infiltration. The spinal root of the fifth nerve shows degeneration by the Marchi method in the medulla oblongata, more intensely in its posterior part. A transverse section was made through the right optic nerve; it shows much degeneration.

The tumor consists of groups of cells separated by bundles of connective tissue. In the dura from the region of the tumor the cells form sometimes elongated masses as seen in an endothelioma.

The small tumor found on the cerebellum at the exit of the seventh nerve, is of very peculiar structure. It appears to have originated in the choroid plexus, and in one portion shows the convolutions of this plexus. It is composed chiefly of neuroglial tissue and contains nerve cells scattered through it irregularly; some of these resemble the cells of the spinal ganglia, others are like the cells of the anterior horns, except that dendritic processes are not so distinct though occasionally they are seen. The tumor is vascular. The cells contain chromophilic elements, though these are not so numerous as is usual in nerve cells. The tumor also contains medullated nerve fibers, as shown by the Weigert hematoxylin stain. These are chiefly at the periphery, but here and there within the substance of the tumor one or two medullated nerve fibers may be seen.

CASE II.—McC., male, aged forty-three years, was referred by Dr. Biddle to Dr. de Schweinitz's service in the University Hospital, and examined by Dr. Spiller February 20, 1906.

He had had severe pain variable in intensity in the head about four months, worse at night, and controlled only by morphine. The pain was in the distribution of the first and second divisions of the right fifth nerve and slightly in the third division. No dizziness was felt. He had been exposed to syphilis about a year previously, and it was uncertain whether he had contracted the disease or not. He complained of diplopia. The hearing had not been so good in the right ear as in the left about two years, but he had had repeated colds. The right side of the head was said to perspire much less freely than the left. The right pupil was smaller than the left. Reaction to light was very sluggish, especially in the right eye; reaction in accommodation was prompt. He was unable to rotate the right eyeball outward, and the right eyeball was slightly retracted; the right palpebral fissure was smaller than the left. The right masseter muscle did not contract so forcibly as the left, and the jaw deviated a little to the right when the mouth was opened.

Gait and station were normal. The bladder and rectum were not affected. The muscular strength was not diminished. The patellar reflex was normal on each side. No objective sensory changes were detected, except that light touch was felt on the right side of the head and face as pain, while heavy pressure was less painful.

A hard, swollen gland was found in the left side of the neck at the anterior border of the sternocleidomastoid muscle.

Dr. Randall found that the reduction in hearing in the right ear was slight, and was caused in part by middle ear disease. The bone conduction was not so good as it ought to be, and a nerve lesion could not be excluded, but the impaired conduction was no more than is common with such old tympanic deafness.

An examination of the eyes in Dr. de Schweinitz service was made February 20, 1906. O.D.,  $\frac{6}{12}$ , with correction,  $\frac{6}{12}$ . O.S.  $\frac{8}{12}$ , +, with correction  $\frac{6}{7.5}$ . Hyperemia of tarsal and bulbar conjunctiva. Internal squint O.D., limitation of movement of O.D. toward right. Pupil of O.S. larger than that of O.D. Paralysis of external rectus of O.D. Both irides respond to light. Ophthalmoscopic examination: O.D. oval disk, temporal half slightly pallid. Low H. O.S. oval disk. Nerve of good tint.

Dr. Harland, in Dr. Grayson's clinic, reported March 17, 1906: He has no sinus pain or tenderness. Nasal obstruction has existed three months. The septum is deviated to the left. Far back on the left side is a soft, bleeding mass, and a similar mass is found in the vault of the pharynx on the right side. The small mass in the vault of the pharynx hanging down on the left side bleeds to the touch. The lateral folds are thickened. The larynx is congested, but not paralyzed. The diagnosis was sarcoma of the nasopharynx.

Dr. Frazier, at my request, removed the enlarged gland of the neck for diagnostic purposes, and it was found to be the seat of an endothelioma. This was done before the report of the examination of the throat was obtained.

The pain in the right side of the head and face continued, and relief by surgical means seemed imperative. Dr. Frazier operated April 5, 1906, and exposed the Gasserian ganglion. Neoplastic tissue was found about it, a part of which with a portion of the ganglion was removed. This removal was followed by excessive hemorrhage, presumably from the internal carotid, and the operation had to be stopped. A provisional ligature was placed on the common carotid artery. The patient was not severely shocked at first by the operation, but an hour later the pulse suddenly became very rapid, reaching 160, and blood pressure became 112. By night the pulse fell to 120 and the blood pressure rose to 120. The man was comfortable the next day.

He complained frequently of pain in the distribution of the right fifth nerve after the operation, but it was not of the same severity as before the operation. Touch was not felt in the distribution of the three branches of the fifth nerve unless it were made with slight pressure, when it was recognized. The right conjunctiva was anesthetic.

May 24, 1906, the patient tried to get out of bed four times, and each time fell to the floor and had to be lifted back to bed. He was out of bed May 25, but was duller than usual. By mid-day he became dizzy while walking, and fell to the floor. He became stuporous and by night was unconscious. Respiration was somewhat labored. He died at 6.30 A.M., May 26. There was some suspicion that he might have obtained an overdose of morphine from some of his visitors.

The brain was very adherent to the dura at the base of the right temporal lobe, and a tumor mass extended from the base of the skull into the temporal lobe. The right temporal lobe was oedematous and very soft, and was torn a little in removing the brain, and still more so by handling the specimen later. The tumor mass was yellowish in color and easily separable from the brain. The brain tissue beneath was very vascular. Recent fluid hemorrhage was in the base of the skull and apparently did not come from the necropsy. One or two recent clots were in the tumor. Death possibly was from hemorrhage. The region of the right Gasserian ganglion was occupied by the tumor, and no distinct ganglion tissue could be found. The case was one of tumor of the right Gasserian ganglion, extending into the base of the right temporal lobe and into the nasopharynx.

My microscopic examination gave the following results:

Teased specimens, stained with osmic acid, of the right twelfth, right eighth, and right seventh nerves were normal. The right sixth nerve showed degenerated fibers in teased preparations.



The descending spinal root of the right fifth nerve was partially degenerated in the medulla oblongata, by the Marchi stain. The right eighth nerve, by acid fuchsin and Weigert stain, was normal. The right sixth nerve was embedded in the tumor and was partly degenerated as shown by these stains; some of the axis cylinders and medullary sheaths were much swollen. The sensory portion of the right fifth nerve was intensely degenerated, as shown by the Weigert method and also when teased and stained in the fresh state by osmic acid.

The tumor had the appearance of an endothelioma. The Gasserian ganglion was embedded in the tumor, and the nerve cells and nerve fibers of the ganglion were much degenerated. Nerve bundles in tissue from the region of the right Gasserian ganglion were intensely degenerated.



FIG. 3.—Photograph of the base of the right cerebral hemisphere from Case II, showing a condition closely resembling that of Case I.

The nerve cells of the ganglion were greatly altered; many were shriveled masses of granular pigment in which no nucleus could be detected, or if the nucleus were present it was indistinct.

The important features of Case I are: Paralysis of the right fifth nerve, with severe pain as the first symptom, then blindness of the right eye, later of the left eye, with optic neuritis, impaired mentality when the pain was severe, inequality of pupils, the right being the smaller, loss of reaction to light probably from the optic nerve disease, bilateral deafness, weakness of the soft palate on the right side, impairment of the sense of smell, loss of patellar and Achilles tendon reflexes, ataxic gait and station, weakness of the left third nerve, still greater weakness of the right third nerve, and paralysis of the right sixth nerve. The facial nerve was not affected.

The possibility of syphilis was at first considered, but later tumor of the Gasserian ganglion was the diagnosis.

The important features of Case II are: The history of a recent exposure to probable syphilis, the pain and weakness in the distribution of the right fifth nerve, impaired hearing on the right side, lessened sweat secretion on the right side of the head, inequality of the pupils, sluggish iridic reaction to light, with prompt reaction in accommodation, weakness of the right external rectus muscle, some retraction of the right eyeball, and narrowing of the right palpebral fissure. Dr. Randall's examination made the right-sided deafness of doubtful diagnostic value, but the discovery of the tumor in the nasopharynx seemed to point to intracranial tumor as the cause of the symptoms. This possibility was strengthened by the excision of the enlarged lymph gland of the neck, and the discovery of the endothelioma within it. The diagnosis made by me was tumor implicating the right Gasserian ganglion, probably endothelioma. The right sixth nerve evidently was affected. The sympathetic paralysis of the right side of the face might be explained by the lesion of the fifth nerve.

Operation did not promise much, because it was evident that the tumor was extensive, was both intracranial and extracranial, and its complete removal was impossible. The pain in the right fifth nerve distribution was so intense that relief must be obtained. Dr. Frazier accordingly operated and removed a part of the Gasserian ganglion.

In the case reported by Dercum, Keen, and Spiller,<sup>2</sup> enlargement of the glands of the left side of the neck, on the side of the trifacial pain, was an early sign, and some of these glands when examined were found to be the seat of endothelioma. The patient had shooting pains in the lower limbs. The patellar reflexes were lost. Pupillary reflexes were normal, there was no failure in rotation of the eyes, each disk was somewhat anemic, and there was no congestion, neuritis, or atrophy. The symptoms of intracranial disease so far as the cranial nerves were concerned were confined to the fifth nerve. The pain in the face was still intense immediately after the first operation. The only change in the objective sensory phenomena was increase in the hypesthesia, except in the conjunctiva and brow. Some time after the first operation paralysis of the left external rectus occurred. In the second operation a large portion of tumor was removed, and still the pain persisted. The entire trigeminal distribution showed increased hypesthesia. The man was still able to appreciate contact, decided differences in pressure, and differences between a spoon dipped in hot and one dipped in cold water. The cornea was absolutely anesthetic. There could be scarcely any doubt that the Gasserian ganglion was entirely removed.

Hofmeister and Meyer have recently written a paper on tumor of the Gasserian ganglion. In their case pain in the distribution

<sup>2</sup> Jour. Amer. Med. Assoc., April 28, 1900.

of the right fifth nerve was the first symptom, then developed weakness of the muscles of mastication on the same side, and loss in objective sensation in this distribution, right-sided choked disk, paralysis of the right third, probably of the fourth, sixth, and eighth nerves. The lymphatic glands on the right side of the neck were swollen.

So much of the tumor as could be removed was excised in this case, and pain ceased entirely, but only for about three months, and then became severe again. A necropsy was not permitted. They believe the implication of the cavernous sinus in the tumor caused the motor disturbance in the right eye and the right choked disk. They think the tumor may have grown into the orbit. From the necropsies in my two cases it seems more probable that the paralysis of the ocular nerves and the choked disks are caused in these cases by direct implication of the nerves in the tumor, and by increase of intracranial pressure, as well as by disease of the cavernous sinus. After the operation their patient was almost entirely unable to chew on the right side, light touch usually was not recognized, pin stick was recognized somewhat better without distinction of head and point.

The diagnosis of a lesion of the Gasserian ganglion is usually easy, but it may be difficult to determine whether it is syphilitic meningitis or a tumor. In the case of Dercum, Keen, and Spiller, and in my Case II, the syphilitic infection was probable. One is tempted by his desires to make the diagnosis of syphilis, knowing that for this affection relief is often obtained in mercury and iodide; whereas in tumor of this region the prognosis is very serious. Tumor of the Gasserian ganglion seems in most cases at least to be irremovable. It apparently has its origin in the dura and has the character of an endothelioma or sarcoma, the distinction between these two forms depending largely on the interpretation of the growth by each investigator. It is usually of large size, and while at first it may be confined to the region of the Gasserian ganglion, it soon extends chiefly as a flat growth, over the base of the middle fossa, possibly into the posterior fossa, and into the orbit. It has a tendency to extend into the base of the temporal lobe above it, as in my Cases I and II, without infiltrating the brain, although firmly adherent to it. This implication gives no symptoms, unless it be the cause of the loss of smell which occurred in my Case I. Loss of smell is not uncommon in brain tumor when intracranial pressure is much increased, but when the base of the temporal lobe is implicated the lesion is near the supposed centre of smell. Endothelioma arising in the dura not infrequently implicates the adjacent bone.

The diagnosis of syphilis is therefore likely to be made, because of the history of syphilitic infection in some of the cases, and because of the knowledge that this disease by the basal meningitis it produces may readily lead to symptoms of implication of the Gasserian ganglion. The mistake in diagnosis is not likely to be so serious as in

tumor of some other location in the brain, as complete removal by operation seems impracticable in most cases at least. In my Case I the pain in the distribution of the fifth nerve was not so severe as in Case II, nor as in the case of Dercum, Keen, and Spiller, and we believed that possibly a decompression, might be sufficient by relief of intracranial pressure to lessen the suffering. The man, however, lived only one day after this operation.

The swelling of the lymphatic glands of the neck from tumor is a valuable means of diagnosing intracranial neoplasm. It is not observed in every case, but was present in the case of Dercum, Keen, and Spiller, in the case of Hofmeister and Meyer, and in my Case II. It is not difficult to excise an enlarged gland, and the finding of tumor within it, endothelioma or sarcoma, is extremely indicative of brain tumor, when such symptoms as those described above are present. The glandular tumor may result from a growth in some other part of the body, but it seems to occur with sufficient frequency in tumor of the Gasserian ganglion to make its presence of diagnostic value.

In some instances the fifth is the only cranial nerve involved, as in the case of Dercum, Keen, and Spiller, and then some confusion in diagnosis with the *tic douloureux* may occur, especially if objective disturbance of sensation in the fifth distribution be slight, as in the case to which reference has just been made. Some disturbance of objective sensation is almost always present, the pain is felt in all three branches of the nerve nearly simultaneously, because the disease is in the ganglion in which these roots arise, and the motor branch of the fifth nerve soon becomes paralyzed. With such a symptom complex the diagnosis of *tic douloureux* is impossible. It is in the early stage of the symptom complex that operation on a tumor of the Gasserian ganglion is more promising, and it is possible to perform the operation while the tumor is small. In any case in which pain is felt in all three branches of the nerve nearly simultaneously and some loss of sensation is detected in the distribution of the same nerve, it is probable that the lesion is in the ganglion, and this probability is increased if paresis of the motor portion of the fifth nerve occurs. It is at this stage that we might hope to remove the tumor entirely. Pain in the fifth nerve is almost always an early symptom, and yet it may in rare instances be slight.

I<sup>2</sup> have studied a case in which each ganglion was embedded in and infiltrated by a soft ependymoma without distinct clinical signs of this invasion. The man had had headache only in the left occipital region extending forward to the left temporal region, and lying on the left side increased the headache. He had had also soreness on pressure over the left supra-orbital and left infra-orbital foramina, but no tenderness over any other exit points of the fifth nerves. There was never any objective disturbance of either the

<sup>2</sup> AMER. JOUR. MED. SCI., July, 1903, and Jour. Nerv. and Ment. Dis., May, 1907.

sensory or motor portion of the fifth nerves. It is exceedingly questionable whether the headache could be attributed to implication of the fifth nerve; it was not present on the right side of the head, and on the left side it began in the back of the head and extended to the frontal region.

Recently I had a case with necropsy in which a glioma of the pons caused symptoms resembling closely those of tumor of the Gasserian ganglion. Pain was not present in the face. The absence of pain in a case such as this should suggest a glioma of the pons, which may not cause any paralysis of the limbs.

The persistence of pain after removal of the Gasserian ganglion in some of these cases is puzzling. It was exceedingly striking in the case of Dercum, Keen, and Spiller, and was observed in my Case II. Hofmeister and Meyer mention the same phenomenon in their case. They acknowledge the possibility of attributing the recurrence of this pain to conduction by the facial nerve, but they think it is more probably caused by extension of the tumor into the central stump of the fifth nerve. The anesthesia of the cornea would seem to indicate that the conduction at least by means of the upper part of the fifth nerve is destroyed, as the eyeball receives no facial fibers. It is difficult also to explain the preservation of objective sensation from peripheral stimulation. In the case of Dercum, Keen, and Spiller, after the second operation hypesthesia of the fifth nerve distribution with anesthesia of the cornea was present. This may indicate that the seventh nerve may convey sensation. In this case hypesthesia was present before the first operation, but the patient could distinguish between the point and head of a pin, and pressure sensation was everywhere well preserved. All handling of the skin of the face gave pain and there was marked hyperalgesia.

In some cases of removal of the Gasserian ganglion for tic douloureux all sensation, including that of pressure, is lost, at least for a period following the operation, but in two cases of removal of the Gasserian ganglion I<sup>4</sup> have observed, preservation of pressure sensation persisted with loss of other forms of sensation in the distribution of the fifth nerve. In some, if not in all, of these tumor cases in which the ganglion is implicated removal of the ganglion or a large part of it does not seem to be followed by complete loss of pressure sensation in the fifth distribution. This preservation of pressure sensation was very remarkable in my two cases, in one of which a large part of the ganglion had been removed, and was observed also in the case of Dercum, Keen, and Spiller. In the case of Hofmeister and Meyer, after the operation light touch usually was not recognized, but pin prick was felt somewhat better without distinction of head and point; this may have been caused by preservation of pressure sensation. Microscopic study of the tissue removed at necropsy

<sup>4</sup> Jour. Nerv. and Ment. Dis., 1906, p. 736.

in my Cases I and II showed intense degeneration by the Weigert medullary stain, of the sensory root of the fifth nerve in both cases. It is true that the Marchi stain showed many fibers in the sensory roots of both cases in the process of degeneration, but this by no means implies that these fibers were capable of conduction, as the Marchi reaction is available for tissue that has been degenerated for months.

I have for a long time believed that the facial nerve may contain some sensory fibers, and in lecturing on this subject in 1907 to the students of the University of Pennsylvania I suggested that a member of the class might make it a subject of special study. The result has been an excellent paper by R. H. Ivy and L. W. Johnson,<sup>5</sup> which contains the evidence pointing to this possibility.

It is unquestionably true that in some cases excision of the Gasserian ganglion causes complete loss of all forms of sensation, but this fact does not make the transmission of certain forms of sensation through the facial nerve impossible. It is not improbable that the deep sensation of the facial nerve may be temporarily interfered with by operation on the trigeminal nerve. Twisting out peripheral branches of the latter causes much swelling of the face, and probably, thereby, some impairment of the function of the facial nerve. Excision of the Gasserian ganglion causes swelling of the axis cylinders and medullary sheaths of the peripheral branches of the trigeminal nerve, and if these are intimately associated with branches of the facial nerve, this swelling may also interfere temporarily with the function of the latter. Destruction of the sensory root of the trigeminal nerve by a tumor affords better opportunity for testing the sensation of the face, than does destruction of some part of this nerve by operation, at least in the period immediately following operation. There is great need of further observation regarding the preservation of pressure sensation in relation to lesions of the trigeminal nerve.

When the pain is intense in these cases, as usually it is, division of the sensory root of the fifth nerve or removal of a part or of the whole of the ganglion when possible is a justifiable operation. It may lessen the pain and in some cases remove it, but it is not an infallible means of relieving suffering. It is true that as yet no complete removal of a tumor of the Gasserian ganglion is on record, but complete and early removal might be possible. Operation, however has been attempted in very few cases.

Very severe hemorrhage followed the removal by Dr. Frazier of a portion of the ganglion in my Case II, possibly because the tumor may have weakened the walls of the vessels, and rendered them more liable to rupture. This fact should be borne in mind in operations on tumor of the Gasserian ganglion, as after the ganglion is cut

<sup>5</sup> Univ. Penna. Med. Bull., May, 1907, p. 35.

from most of its attachments it is customary to pull it away, and repeatedly a rupture of the cavernous sinus has occurred. It might be well to avoid all pulling on intracranial tissue when operation is performed on tumor of the ganglion, except tearing the sensory root from the pons. This would be the most desirable procedure when the tumor could not be removed.

Hofmeister and Meyer<sup>6</sup> give the literature on tumor of the Gasserian ganglion. It is not very extensive. In their case the tumor was a sarcoma. Marchand<sup>7</sup> has made the pathology of these growths recently a subject of special study. The cases he collected with necropsy are those of Günsburg, Blessig, Petrina and Klebs (two cases), Goodhart, Hansch and Bezold, Krogius, Hegelstam, Prince; Dercum, Keen, and Spiller, and Hofmeister and Meyer. To these Marchand adds another case. It seems remarkable that the cases of tumor of the Gasserian ganglion are not more numerous. I can only believe that these tumors are not diagnosticated in many instances when they exist.

The first operation for tumor of the Gasserian ganglion was done by Krogius.<sup>8</sup> An endothelioma the size of a pigeon's egg was removed, but a portion was left behind. In this case the tumor presented in the nasopharynx. Death occurred from meningitis thirteen days after the operation.

The tumors in my two cases have much the appearance of an endothelioma. As Marchand points out, the newgrowths of the Gasserian ganglion that have been reported seem to have a very similar histology, although different names have been given to them. He is inclined to believe that these tumors arise in the undifferentiated *Anlage* of the ganglion, and that they may be regarded as neurozytomas. In this connection it is interesting to refer to the neuroglioma found in my first case at the junction of the pons with the cerebellum, and distinct from the tumor of the Gasserian ganglion. It may have been a congenital anomaly, and gave little evidence of growth, and was very small. It may afford some support for the opinion that in these cases of tumor of the Gasserian ganglion there is a portion of the *Anlage* of the ganglion which fails to become differentiated into ganglion tissue, and later becomes the seat of a neoplasm. In whatever way these tumors are regarded, the necropsies show that they are malignant, and that they are likely to invade the bone of the skull.

<sup>6</sup> Deut. Zeit. f. Nerven., 1906, xxx, 206.

<sup>7</sup> Festschrift f. von Rindfleisch, 1907, p. 265.

<sup>8</sup> Rev. de chir., 1896, xvi, 434.

## THE ETIOLOGICAL IMPORTANCE OF ABNORMAL FOOT POSTURE IN AFFECTIONS OF THE KNEE.<sup>1</sup>

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IN all ages builders have realized the importance of a secure foundation, and the "man which built his house upon the sand" has been justly held up to ridicule. In the human frame the foot is essentially the foundation of the body, and mechanical principles are similarly involved, although modified, it is true, by the adaptability of the muscular system. When, however, muscular control weakens, the natural and acquired errors in the structure become apparent and produce symptoms which are easily understood, if viewed in the light of mechanical laws.

Despite the great amount which has been written about the weak foot, few, if any, of the ills to which flesh is heir are more poorly treated; and such will continue to be the case as long as it is deemed sufficient to send the sufferer to the instrument maker for "a pair of plates." To him who aims at the cure of the affection by the restoration of normal function, the available literature furnishes all that is necessary. One of the more remote effects of the weak foot, however, while mentioned by various writers, has not in my opinion received the emphasis which it merits. Through the abnormal position of the foot an excessive strain is thrown upon the knee and its muscles, which may not only give rise to pain in and around the joint, but, if unrelieved, may also produce actual joint changes; further, strain due to such abnormal foot posture may be a very potent factor in keeping up disability of the knee-joint due primarily to other causes.

The references in the literature to this phase of the subject are practically limited to a few works on orthopedic surgery and to several special articles.

In speaking of the more or less unusual symptoms of flat foot, Bradford and Lovett mention the occurrence of pain and a feeling of strain at the insertion of the hamstring tendons, pain and irritability of the knee with, in some cases, recurring attacks of synovitis, and occasionally backache. Whitman states that there may be "pain in the knee, hip, or lumbar region, symptoms more common in women than in men." Dane, in an excellent paper on the mechanics of the subject, definitely locates various points of pain above the ankle, and Stone also refers to them. In an analysis of 1000 cases of static foot trouble, Blodgett noted pain in the knee in 73 cases; in 21 cases the pain was wholly above the ankle, and of

<sup>1</sup> Read at a meeting of the Pittsburgh College of Physicians, February 27, 1908.



these, "13, or more than half, had pain only in the knee, usually over the internal condyle, and 4 others had pain in the knee associated with pain elsewhere above the ankle;" he calls attention to the fact, moreover, that knee symptoms are more common than his analysis would indicate, since cases of villous arthritis, due to flat or pronated feet, were not included in his series. In view of these statements, it is rather surprising to find no mention of pain above the ankle in several of the recent American and German orthopædic text-books.

As regards the production of definite joint changes, Goldthwait says that chronic villous arthritis of the knee "is very commonly associated with, and is undoubtedly in part due to, flat foot, the weakness here having resulted in strain and weakness at the knee." In the same connection Painter and Erving state: "Flat and pronated feet, by causing strain to the internal lateral ligaments of the knee, are common causes of congested and hyperemic knees, particularly in stout and flabby individuals, usually women."

The value of a corrected foot posture in recurrent dislocation of the internal semilunar cartilage is recognized by Robert Jones and by Lovett, but I have failed to find any reference to its value in other affections.

When studied from the mechanical standpoint, the reasons for the production of symptoms at the knee by a weak foot are clear and distinct. Such symptoms are due indirectly to the inherent instability of the knee and directly to: (1) Strain exerted laterally on the internal lateral ligament, and (2) strain due to interference with the normal rotation of the femur on the tibia; their time of appearance and severity are dependent upon the muscular control.

**INHERENT INSTABILITY OF THE KNEE.**—"The knee is a joint depending entirely upon the ligaments for its strength. Disregarding the patella, there are only two small articular areas in contact in all positions of the limb. . . . There is neither cup nor socket nor real concavity of any sort. . . . The two bones with the articular cartilages left on and all the ligaments removed are in unstable equilibrium in all positions. This mechanical disadvantage and the arrangement of the lubricating apparatus, which is at times inadequate and at times an absolute obstacle to the working of the joint, furnish the chief reasons why the knee is the most frequently deranged of all the joints in the human body" (Tenney).

**LATERAL STRAIN.** There are normally a few degrees of divergence of the thighs, and this is more marked in women than in men on account of the greater width of the pelvis; as Lovett expresses it, "Some degree of knock-knee is anatomic." This necessarily produces a slightly greater strain upon the structures on the inner side of the knee. The assumption of the so-called "attitude of rest," in which the feet are separated and everted, increases this strain in proportion to the degree of pronation (rolling in of the ankle) which

occurs. It is further increased in walking with the legs in outward rotation, since in this position the line of motion of the knee-joints diverges from that of the body. That the force thus exerted upon the internal structures of the knee is one to be reckoned with, is evident, since it is sufficient in susceptible individuals to produce the deformity of knock-knee, to which, in some cases, at least, flat foot stands in causal relation, and the correction of which in the milder degrees is possible by throwing the weight on the outer edge of the foot.

**INTERFERENCE WITH NORMAL ROTATION OF THE FEMUR ON THE TIBIA.** The axis of the ankle-joint is directed slightly downward and backward; in the normal foot, according to Dane, the two axes meet in the horizontal plane in an angle open backward of 169 degrees and in the vertical plane in an angle open downward of 154 degrees. This divergence is of undoubted assistance in maintaining the upright position with a minimum of muscular effort. At the knee the final act of extension consists in a gliding backward of the larger, inner condyle, so that the femur is rotated inward on the tibia; similarly, the beginning of flexion is accompanied by a rotation outward of the femur (Quain); this aids in maintaining the knee in extension. Into the mechanism at the hip it is not now necessary to go.

In the assumption of the weak- or flat-footed position, the foot moves inward and downward at the mediotarsal joint, while the heel and the ball remain fixed. This has two effects: (1) The divergence of the axes of the ankle-joints is diminished, and the assistance thereby afforded in the maintenance of the upright position is decreased or lost; and (2) the tibia, which participates in the movement, rotates inward, thus "interfering to a great extent with the operation of the mechanism by which complete extension of the knee should lock the joint and render it proof against the constant tendency of the body weight to flex it" (Dane), thus necessitating the constant exercise of muscular force.

**MUSCULAR SUPPORT.** Normal muscular tone is the prerequisite of a normal posture and a normal gait, and as long as it exists, mechanical defects of a considerable degree may be present without producing symptoms. With diminishing muscular power, the individual tends to assume a posture in which more and more weight is transferred to the ligaments, and under such circumstances slight deviations from the normal become active. Hence it happens that the conditions under discussion are seen in children who have grown rapidly, in the weak and debilitated from any cause, and in the abnormally stout.

As an example of the subject, one may picture the amount of traumatism (to the knees) sustained during the afternoon's shopping expedition of a short, very stout, and correspondingly flabby individual with pronated or flat feet, and wearing the conventional French heel, whose already too small base is more or less

rounded by use; imagine for a moment the repeated injuries that occur from the standing before the counters, the walking over uneven streets, the clambering up and down the very high steps of our streets cars, and possibly the half hour's clinging to the strap while she is jerked this way and that with every movement of the car. With such a complicated joint as the knee the wonder is that any such escape.

Insistance must also be laid upon the fact that in the normal individual a knee which has been injured, either by traumatism or disease, is in exactly the same condition as if the individual were generally weakened. The relaxation of joint structures, which naturally follows inflammation, and the muscular atrophy from disuse render the joint more susceptible to injury. Under such circumstances, in an exactly similar manner, slight deviations from the normal foot posture may throw sufficient strain on the knee to retard or even prevent recovery. In such cases correction of the foot error may bring immediate improvement. It is my opinion that in all cases of primary knee-joint affections any apparent defect of the foot should be corrected, and that in cases of long standing, even in the absence of any apparent defect, the weight should at least be transferred to the outer side and the foot brought into the adducted position. If such details were more carefully carried out in the treatment of acute affections of the knee, it is safe to say that fewer chronic troubles would be seen.

The following cases are presented as examples of this condition; others might be cited, but these are sufficient to illustrate the various types:

CASE I.—Mrs. F. G., referred by Dr. James I. Johnston, was seen February 16, 1906. She had first noticed soreness in the right knee about a year and a half before, following extra exertion, and a few weeks after an attack of tonsillitis; two or three weeks later the left knee also became affected. Some puffiness about the joints and "grating" were noted; there was no pain any place else. No benefit had followed a rest in the country nor massage and salt baths at Atlantic City. She now complained of pain up and down the legs, chiefly in front. On account of her circumstances she was obliged to be on her feet a great deal, and was also under considerable nervous strain. The patient was a fleshy, middle-aged women in fair general condition. There was slight fullness on each side of the patella tendons and above the patellæ; no demonstrable fluid; no palpable fringes; slight crepitation; on the right knee there was tenderness over the internal lateral ligament. The feet were markedly everted in walking and there was marked pronation; double hallux valgus of moderate degree was present; the heels of the shoes were small and high.

The knees were supported by flannel bandages, and electricity and compresses were used. The shoes were changed so as to give

a firm base of support and to correct the pronation, and the arches were supported. Improvement was gradual but steady, and when last seen, in May, the patient was quite comfortable.

CASE II.—Mrs. J. D. F., referred by Dr. James P. McKelvy, was first seen June 19, 1907. She had been troubled with stiffness of the knees, especially the left, for two or three years; pain had been absent until the last few weeks, and about a week ago became especially severe in the left knee; the knees were “puffed out on the sides” at night. She had noticed that she was worse when she sat a good deal or ran the machine. The stiffness was the especial complaint.

The results of examination in this case were similar to those in Case I, except that there was considerable swelling (synovial) of the left knee.

Treatment consisted of several weeks' fixation of the left knee in a splint, hot and cold douching, bandaging, etc., and the correction of the foot condition as in Case I. When last seen, in August 1907, the patient was in good condition.

Cases I and II represent the type of congested knees (in some cases going on to villous formation), which are seen in stout, flabby individuals, with flat or pronated feet.

CASE III.—J. S., a male, aged eight years, was referred by Dr. W. W. Jones on account of trouble with the right knee. He was first seen on December 18, 1905. About two years and a half ago, following kneeling on the wet ground, the right knee became swollen and painful, and he was in bed for about two weeks, although not especially inconvenienced. Fifteen months later there was a second attack of pain and swelling, and he was in bed again for a time. Within the last six months he has had trouble three times. His present trouble dates from three weeks ago, when he had a fall, and was supposed by the friends to have put the knee out of joint; several days before coming to see me he had struck it again, and had complained greatly of pain, although he had continued to use it. He had limped slightly for about a week.

The patient was a slender lad in not very good general condition. The right knee was a quarter inch less in circumference than the left (he had been wearing an elastic knee-cap), but the thigh and calf were a half inch larger. There was some spasm of the hamstring tendons. No apparent abnormality of the joint could be detected, except that there was a slight degree of relaxation of the ligaments. The feet were plainly weak, and there was noticeable twitching of the muscles during standing; there was in-toe and considerable pronation.

Treatment consisted in support to the knee by a flannel bandage, the alternate hot and cold douche, correction of the abnormal foot posture by changes in the shoe, and later, when the spasm had disappeared, the use of exercises to build up the leg muscles. Up to

February, 1908, when last seen, the patient has experienced no further trouble.

CASE IV.—Miss A. G., aged seventeen years, consulted me May 29, 1906, in regard to pain in the right knee. About four years ago she had twisted the foot and hurt the knee, and since then had "hurt" it at various times, losing a day or two. Pain is referred to the outside of the knee, is dull in character, and lately has run up to the hip; there has also been some pain below the knee; no history of locking or grating; a little swelling has been noted at times.

Here also examination failed to reveal any abnormality in the knee, but the weakness of the feet was at once apparent when the patient walked across the room; the feet were markedly pronated and the toes showed the marks of compression by the improper shoes. Correction of the foot error by a proper shoe, the use of appropriate exercises, and instruction in walking gave immediate improvement, and when seen about a year later, the patient had experienced no further trouble.

CASE V.—S. S., male, aged eighteen years, consulted me October 20, 1907. About a year ago, without any known cause, he noticed swelling of the left knee around the patella, which disappeared under bandaging; there was no redness, no pain, and no interference with motion. He has continued to wear the bandage and the knee seems to be getting weaker. During the last few weeks there has been some pain on the inside of the knee, but no sudden sharp pain, no locking, and no interference with motion. He has noticed at times some stiffness in the arch of the foot, and has a tendency, which he cannot explain, to stand on the outer edge of the foot.

There was marked varicose veins on both legs. The left knee was slightly (not over a quarter inch) larger than the right; the calf was a half inch larger. There were no tender points about the knee and nothing to be felt, except crepitation in the joint. The left foot presented a marked degree of distortion during use, the mediotarsal joint being displaced inward and downward with each step.

The alternate hot and cold douche, a corrective heel, a Whitman arch support, and exercises were prescribed.

When seen ten days later, all discomfort in the knee had disappeared, and when last seen, in December, 1907, there had been no return.

Cases III, IV, and V are of especial interest because of the very early age at which knee symptoms appeared and the very prompt and permanent response to the correction of the static foot error. In these cases the condition was simply one of strain without the production of joint changes.

CASE VI.—R. H. W., referred by Dr. George Wright, was seen March 5, 1907. Five months before he had twisted the right knee through a fall; there was not much swelling or pain and no ecchy-

mosis. A week later, ordinary measures having been used in the meantime, he returned to his home in Boston, where his family physician found effusion into the joint and applied a cast, following which the effusion disappeared in about two weeks; in addition to the fixation he had some massage. When he left Boston he was still limping and motion was limited. After a few months he could walk a mile without discomfort, but more brought on pain just to the inside of the patella, and in the calf and up the leg; there was also some pain in the heel. About two months ago he noticed crepitation. A bone-setter diagnosticated a dislocated tendon and replaced(?) it without apparent effect. He complains most of pain on the inside of the leg near the knee.

The patient was a muscular young adult with noticeable general looseness of the joints. There was considerable atrophy of the leg, but no demonstrable change in the joint; in standing, the right knee was not so fully extended as the left, which, indeed, was slightly recurved; the discomfort of which he complained was located definitely over the inside of the joint. Both feet were markedly pronated and everted, and there was a marked excursion downward and inward at the mediotarsal joint at each step; this postural defect had evidently been present for years.

The knee was treated in a similar manner to that in the previous cases, and the defect of the foot was corrected by changes in the shoe and by a felt pad under the arch. Improvement was soon apparent. Later, when he was going into the woods for a vacation, a steel arch support was made for him, with which he went through an active hunting and fishing trip without discomfort.

After resuming office work, however, there was a slight but persistent return of the discomfort. A course of massage brought up the size of the leg to about that of its fellow, but failed to relieve all the trouble. The patient then volunteered the information that he had less discomfort after walking a long distance than when engaged in less active exercise, as, for example, after billiards. Following out this suggestion, he was allowed to engage actively in walking and other sports, and when last heard of had walked five miles without inconvenience and had been dancing.

Case VI is of interest because of the two points which it illustrates. The static foot error had been present for years without producing symptoms until the resistance of the knee was lowered by injury; then it played a very definite part in preventing full recovery. The general looseness of the joints had also caused no inconvenience, no doubt on account of the excellent muscular development; with the lowering of the muscular tone from disuse, however, this looseness also became an active factor in retarding complete recovery.

CASE VII.—T. P. McD., an ironworker, consulted me September 6, 1907. Two months before he had been struck just above

the left patella by a "reverse lever." The knee began to swell in a few hours, but there was no ecchymosis; he was in bed for about a week (but without a splint), and since then has used a cane. He now has most pain in the mornings and gets very tired toward evening; there is some swelling and what he describes as "a catching" below the knee; he complains a great deal of a twitching of the muscles on the front of the thigh; he can walk but a short distance and cannot go up steps.

The patient was a very muscular young adult, in excellent general condition. The left knee was very slightly swollen, chiefly in the region of the infrapatellar pad. The patella floated moderately. The point of tenderness complained of was just above the patella, where he had been struck. There was no apparent abnormality below the knee.

On account of the evidence of fluid in the joint, the knee was first baked and strapped with the adhesive strapping, but, as the strapping produced several large blisters, this was discontinued and the knee put on a splint; massage, electricity, and, later, alternate hot and cold douching were then used. Improvement was not so rapid as was expected, however. After several weeks, although there was no apparent postural defect, the effect of raising the inner edge of the shoe and supporting the arch (by a felt pad) was tried. Both at the time and afterward the patient was very definite in this statement that this "felt better," and improvement was so much more rapid after this that I feel certain it was a valuable adjunct in treatment.

Case VII is important, it seems to me, in suggesting the value of the more general use of temporary support (Thomas heel or felt pad) to the arch in the treatment of injuries of the knee, and since the measure is such a simple one, there is no good reason why it should not be employed.

CONCLUSIONS. 1. The production of symptoms at the knee by abnormal foot posture is easily explained by mechanical laws.

2. Pain in or around the knee may exist unassociated with pain in the foot.

3. Strain at the knee from abnormal foot posture may, if unrelieved, produce actual joint changes.

4. Such strain may also be a potent factor in keeping up disability of the knee-joint due primarily to other causes.

5. In all cases of primary knee-joint disease apparent defects of the foot should be corrected, and in resistant cases, especially old traumatisms, even when no apparent defect is present, the transference of the weight to the outer border of the foot is recommended.

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## THE RICIN METHOD OF JACOBY-SOLMS FOR THE QUANTITATIVE ESTIMATION OF PEPSIN.

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(From the private laboratory of Dr. John H. Musser.)

THE various methods for the quantitative determination of pepsin in the gastric juice are numerous and ingenious, although but few have survived the test of time and corroboration. The older methods of Brücke, Grützner, Jaworski, Hammerschlag, and Oppler are of interest but of no practical value, while the Mette method has been and is still being so extensively assailed that its position, despite the advocacy of Pawow, seems to be uncertain. The above-named methods have been so frequently described that the omission of their review may be dispensed with.<sup>1</sup>

In 1906, Jacoby,<sup>2</sup> while engaged in a research on ricin, found that a solution of this substance in 1 per cent. sodium chloride solution became cloudy owing to the insoluble albuminous body contained in the substance, but that if pepsin were added to it the solution cleared up rapidly and completely. Jacoby hinted at the clinical application of this observation, but no attention was given the subject until Solms, working under Jacoby, published his paper the following year.

In this article he gives in clear detail the description of his method which he claims is easy, practicable, and inexpensive, and apparently does away with many of the difficulties surrounding the Mette test.

<sup>1</sup> For bibliography see Farr and Goodman, Archives of Internal Medicine, 1908, i, 648.

<sup>2</sup> Arb. a. d. path. Institut. su Berl., Feiler, Johannes Orth, Berlin, 1906, p. 655.



The following description of Solms's technique is copied from the paper of Farr and Goodman. The only materials needed are a solution of ricin and a  $\frac{n}{10}$  hydrochloric acid solution.

"The ricin solution is made by dissolving 0.5 gram of ricin in 50 c.c. of 5 per cent. sodium chloride solution and filtering. (The ricin used by Solms was obtained from the Vereinigte chemische Werke, Charlottenburg, Salzufer 16, costing 2 marks for 10 grams. Solms preferred this preparation of ricin to Merck's, principally on account of the limited supply, and the great cost of the latter.) The filtered ricin solution has a somewhat cloudy appearance, but on the addition of 0.5 c.c. of  $\frac{n}{10}$  hydrochloric acid becomes decidedly milky. The milky appearance is cleared up by pepsin.

"His technique is as follows: The gastric juice is obtained by extracting the stomach contents one hour after the ingestion of an Ewald-Boas test breakfast. He tests this for the presence of free hydrochloric acid, then determines the total acidity, and in appropriate cases examines for lactic acid. According to his findings he makes varying dilutions of the contents with distilled water. In cases of hyperacidity he dilutes the filtered contents from 1 to 100 to 1 to 10,000, whereas in cases of anacidity or subacidity the dilutions vary from 1 to 10 to 1 to 100. In normal cases he dilutes from 1 to 100 to 1 to 1000.

"In each of five test tubes he puts 2 c.c. of the filtered ricin solution; then with another graduated pipette he adds 0.5 c.c.  $\frac{n}{10}$  hydrochloric acid, which causes the mixture to become very cloudy. Having numbered the test tubes, 1, 2, 3, 4, and 5, he puts in the first tube 1 c.c. of boiled gastric juice; in the second, 0.9 c.c.; in the third, 0.8 c.c.; in the fourth, 0.5 c.c.; and in the fifth, 0 c.c. Then he takes the unboiled juice and, having diluted 1 c.c. of juice with 99 c.c. of water, he puts in the first tube 0 c.c.; in the second, 0.1 c.c.; in the third, 0.2 c.c.; in the fourth, 0.5 c.c.; and in the fifth, 1 c.c., so that in each tube there are 3.5 c.c. of fluid. The test tubes are then corked and put in an incubator, where they are allowed to stand for three hours; at the end of this time they are taken out and the tubes examined to see with what dilution the ricin has been cleared up. If an incubator is not at hand, the tubes can be left at room temperature, of course, for a correspondingly longer time.

"In order to obtain a convenient expression of the pepsin contents of a gastric juice, he designates that amount of pepsin contained in 1 c.c. of a 1 to 100 dilution, which is capable of clearing up the ricin solution after three hours' standing in an incubator, as 100 pepsin units. This he has decided on as the normal standard, because after many examinations of specimens of normal acidity he found the ricin to be cleared up by 1 c.c. of a solution diluted 1 to 100."

Solms divided the specimens of gastric juice according to the

acidity as follows: Normal, "almost normal," anacidity or subacidity, and hyperacidity. Under normal acidity are cases showing a positive reaction for free hydrochloric acid with Töpfer's test and Congo paper, and a total acidity of between 40 and 60. "Almost normal" are cases showing a total acidity between 30 and 40, and 60 and 70, with presence of free HCl. Below these values are cases of anacidity or subacidity, and cases showing a total acidity above 70 he calls hyperacidity.

He reports 12 cases of normal acidity, seven of which showed 100, four, 200, and one, 500 pepsin units, and concludes that pepsin units between 100 and 200 may be considered as the normal. Six cases of "almost normal" gastric acidity (between 30 and 40) showed the same thing as did six cases between 60 and 70. In twenty cases of subacidity there was a marked diminution of pepsin units, generally between 10 and 20 units, in some cases below this, so that the amount of pepsin could not be estimated. Thirteen cases of hyperacidity showed a normal pepsin value and in but two cases was the amount of pepsin abnormally high, once 1000 units and in another instance 500 units.

Witte<sup>4</sup> has published a series of 50 patients on which the estimation of pepsin was made by means of ricin and believes the Jacoby-Solms method is exact and simple and is to be strongly recommended. He alters the technique very slightly, suggesting for normal cases a tube containing a dilution of 1 to 50, and in hypoacidity diluting the gastric juice 1 to 1, 1 to 10, 1 to 20, etc. He believes in this way he can detect minimal amounts of pepsin. Witte has not followed the classification of Solms as to "almost normal" cases, but arranges his series in normal, sub- or anacidity, and hyperacidity. His conclusions are in the main the same as Solms' and he recommends the method very strongly. He queries, however, if there is not a grave source of error, inasmuch as there is no uniform acidity in the test tubes, and he thinks the optimum acidity is disturbed. He suggests for exact scientific work, a neutralization of the acid then by the addition of decinormal hydrochloric acid bringing the acidity to a uniformity. For clinical purposes, however, this not necessary.

Gross<sup>5</sup> objects to the ricin method on one point, and that is that the ricin used by Solms is very impure and there is no way of determining just how much albuminous substance is contained in it. This would seem to be a valid objection, but so far has not been fruitful of error as Solms, Witte, and I have obtained similar results, each working with separate specimens of ricin.

Solms is particularly insistent that studies with his method be carried out according to his description, in order that comparative studies may be obtained, which may be of value in diagnosis and therapeutics of gastric diseases. In our series of cases we have

<sup>4</sup> Berl. klin. Woch., 1907, p. 1338.

<sup>5</sup> Ibid., 1908, p. 643.

followed to the minutest detail Solms' directions, and while not varying from it have chosen in many cases to report the total acidity, free acid, combined acidity, and the acid salts. Control of Solms' method by means of the Mette test was made in ceratin cases by Dr. Farr and reported by us in connection with another phase of pepsin determination.<sup>6</sup> The arrangement of our tables differs slightly from that of Solms inasmuch as we do not favor "almost normal." This seems to be an injudicious subdivision, and we prefer to call gastric juice with total acidity between 40 and 60 normal, and below or above the subacidity or hyperacidity respectively.

TABLE I.—NORMAL ACIDITY (40-60).

Serial number.	Total acidity.	Free HCl.	Combined HCl.	Acid salts.	Ren-nin.	Ricin.	Mette.	Diagnosis.	Case number.
1	40	30	5	5	+	100-200	3.8 (14.4)	Hyperchlorhydria.	464
2	44	26	2	16	+	200	3.2 (10.2)	Gastro-enteroptosis.	505
3	45	20	20	5	+	100	Not made.	Gastric neurosis.	663
4	48	10	26	12	+	100	4.9 (24.0)	Chloro-anemia.	311
5	50	18	14	18	+	10	3.9 (15.2)	Chronic gastritis.	570
6	50	30	15	5	+	200	4.4 (19.4)	Migraine; dilatation of stomach.	511
7	54	34	18	12	+	100-200	4.3 (18.5)	Gastric neurosis.	434
8	54	36	8	10	+	100	Not made.	Tuberculous enteritis.	659
9	56	24	18	14	+	100	Not made.	Cholecystitis.	884
10	58	30	16	12	+	100	3.7 (13.7)	Hyperchlorhydria.	402
						not clear			
11	58	34	16	8	+	100	3.0 ( 9.0)	Neurasthenia; gastric neurosis.	449
12	60	45	5	10	+	100	5.2 (27.0)	Cholecystitis; hyperchlorhydria.	791

Normal acidity (40 to 60). In these cases we have found the pepsin unit to be between 100 and 200 and agree with Solms in regarding this as the normal. Using the Mette test as a control we have found a certain parallel between the two, both giving normal values, although the ricin method does not show the finer variation disclosed by the Mette method (Table I).

TABLE II.—SUBNORMAL ACIDITY (BELOW 40).

Serial number.	Total acidity.	Free HCl.	Combined HCl.	Acid salts.	Ren-nin.	Ricin.	Mette.	Diagnosis.	Case number.
1	35	0	15	20	0	10-20	2.3 ( 5.3)	Endarteritis; chronic tuberculosis.	140
2	28	6	14	8	Slow.	10	2.8 ( 7.8)	Cholelithiasis; gastritis.	251
3	26	0	..	..	..	20-50	2.0 ( 4.0)	Polycythemia; chr. gastritis (vomitus).	814
4	26	8	6	12	Slow.	10-20	3.3 (10.9)	Gastric neurosis.	579
5	25	0	0	0	Very slow.	10	0.8 (0.64)	Pyelitis.	189
6	22	0	..	..	..	10	1.0 ( 1.0)	Lactic acid +; chronic gastro-enteritis.	813
7	22	0	0	0	+	0	3.4 (11.6)	Chronic gastritis.	571
8	20	0	0	0	0	0	0.1 ( 0.1)	Anacidity.	576

<sup>6</sup> Loc. cit.

TABLE III—HYPERACIDITY (ABOVE 60).

Serial number.	Total acidity.	Free HCl.	Combined HCl.	Acid salts.	Renin.	Ricin.	Mette.	Diagnosis.	Case number.
1	62	30	22	8	+	100-200	Not made.	Goitre; dilated stomach.	871
2	62	34	6	22	+	100	2.8 ( 7.8)	Psoriasis; ecsema.	520
3	62	36	20	6	+	100-200	4.1 (16.8)	Gastric neurosis.	300
4	62	16	40	6	+	10	3.8 (14.4)	(Vomitus); carcinoma pylorus.	227
5	64	40	20	4	+	100	3.3 (10.9)	Neurosis.	575
6	64	30	24	10	+	100	Not made.	Nephritis; gastritis.	824
7	64	48	10	6	+	100	3.1 ( 9.6)	Adhesions; hyperchlorhydria.	615
8	65	40	5	20	+	100-200	3.6 (13.0)	Glycosuria.	500
9	65	40	15	10	+	100	3.4 (11.6)	Syphilis; neurasthenia.	176
10	66	40	11	15	+	100	2.8 ( 7.8)	Myalgia.	680
11	66	36	22	8	+	100	3.2 (10.2)	Tachycardia.	236
12	66	40	20	6	+	100	Not made.	Gastroptosis; gastric neurosis.	225
13	68	24	29	15	+	200	3.6 (13.0)	Frontal sinusitis; neurosis; hyperchlorhydria.	423
14	68	42	20	6	+	200	4.3 (18.5)	Gout; neurosis; alcoholic gastritis.	496
15	68	34	26	8	+	100	3.3 (10.9)	Pancreatitis; hyperchlorhydria.	356
16	68	46	16	6	+	not clear. 100-200	4.6 (21.2)	Cholecystitis; gastric ulcer.	322
17	68	44	6	18	+	100-200	5.9 (34.8)	Chronic appendicitis; gastric neurosis.	757
18	70	40	25	5	+	100	Not made.	Jaundice; cholecystitis.	664
19	70	40	15	15	+	100-200	4.0 (16.0)	Gastritis; hyperchlorhydria.	734
20	70	54	15	1	+	1000	5.8 (33.6)	Hour-glass contraction of stomach; pyloric adhesions.	282
21	70	46	12	12	+	100	3.2 (10.2)	Fibroid of uterus; hyperchlorhydria.	371
22	74	44	22	8	+	100	4.7 (22.0)	Hyperchlorhydria; pylorospasm; cholecystitis; chronic appendicitis.	335
23	75	55	15	5	+	100	3.0 ( 9.0)	Hyperchlorhydria.	538
24	75	40	10	25	+	100-200	3.0 ( 9.0)	Exophthalmic goitre.	455
25	76	30	32	14	+	100	4.0 (16.0)	Appendicitis.	326
26	78	56	20	2	+	100	3.5 (12.3)	Chronic appendicitis.	593
27	78	64	2	12	+	1000	3.8 (14.4)	Appendicitis; hyperchlorhydria.	476
28	78	36	26	16	+	100	3.9 (15.2)	Hyperchlorhydria.	450
29	78	40	16	22	+	100	3.8 (14.4)	Gastric ulcer.	430
30	80	55	15	10	+	100	3.4 (11.6)	Hyperchlorhydria.	678
31	80	55	20	5	+	100	3.0 ( 9.0)	Hyperchlorhydria.	585
32	82	52	18	12	+	100	3.0 ( 9.0)	Hyperchlorhydria.	T.T.M.
33	82	52	14	16	+	100	3.8 (14.4)	Bronchitis; gastritis.	599
34	82	54	24	4	+	100	3.4 (11.6)	Gastritis.	689
35	84	52	28	4	+	100	3.1 ( 9.6)	Hyperchlorhydria.	T.M.B.
36	84	60	20	4	+	100	Not made.	Neurosis; hyperchlorhydria.	883
37	85	35	35	15	+	100	2.9 ( 8.4)	Neurasthenia; gastroptosis.	692
38	85	55	25	5	+	100	2.6 ( 6.8)	Gastric neurosis.	667
39	86	48	28	10	+	100	4.9 (24.0)	Gastric neurosis.	561
40	86	58	2	26	+	100	5.2 (27.0)	Appendicitis; hyperchlorhydria.	273
41	88	54	22	12	+	500	2.8 ( 7.8)	Cholecystitis; hyperchlorhydria.	171
42	88	58	24	6	+	100-200	4.9 (24.0)	Frontal and ethmoidal sinusitis; hyperacidity.	785
43	88	62	12	14	+	1000	5.3 (28.0)	Gastritis; hyperchlorhydria.	334
44	95	60	25	10	+	500	3.1 ( 9.6)	Neurosis; hyperchlorhydria.	489
45	100	45	20	35	+	100	2.9 ( 8.4)	Gastric ulcer.	597
46	106	94	10	2	+	100-200	Not made.	Cystitis; enteritis.	828
47	110	62	32	16	+	200	3.7 (13.7)	Epilepsy (?).	713

Subnormal acidity, below 40. Here again we agree with Solms, as there was a marked reduction of pepsin units co-relative with diminished acidity. The Mette method also gave low pepsin value with the exception of two cases, Nos. 4 and 7, in which the amount was normal. This discrepancy between the two methods is more apparent than real, however, as the control tests used for the Mette estimations were also high (Table II).

Hyperacidity above 60. In 5 cases Nos. 20, 27, 41, 43, and 44 the pepsin value was high. That this sometimes occurs has been pointed out by Solms, but in the majority of cases our results showed normal pepsin units. The Mette test in Cases 20 and 43 was also high, whereas in Case 27 it showed a normal value. In Cases 41 and 44 the Mette was low, which is explained by the low result obtained in the control experiment (Table III).

We have thus been able to study the estimation of pepsin by the Jacoby-Solms method in a large series of cases, and we can corroborate Solms' findings. The method is extremely simple, cheap, and sufficiently accurate for all clinical purposes. The rapidity with which one obtains a result is not the least important factor in advocating its use by clinicians. That it does not possess the finer variations of the Mette method cannot be denied, but in the present state of our knowledge of pepsin this cannot be offered as an objection, as this so-called advantage has been of no help to us in diagnosis.

Experiments were made in a limited number of cases to determine if a uniform acidity made any difference in the final result, and whether the law of Schültz held good for the ricin method. So far both of these questions must be answered negatively.

CONCLUSIONS: (1) The normal pepsin unit as disclosed by the ricin method is between 100 and 200. (2) Cases of hyperacidity with few exceptions are not accompanied by a corresponding increase of pepsin. (3) Cases of subacidity are invariably associated with a diminution of pepsin. (4) The ricin method is to be recommended on account of its simplicity, cheapness, accuracy, and rapidity.

## REVIEWS.

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**ANATOMY, DESCRIPTIVE AND SURGICAL.** By HENRY GRAY, F.R.S., Fellow of the Royal College of Surgeons; Lecturer on Anatomy at St. George's Hospital Medical School, London. Seventeenth Edition, thoroughly revised and re-edited, with additions, by JOHN CHALMERS DA COSTA, M.D., Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College, Philadelphia; and EDWARD ANTHONY SPITZKA, M.D., Professor of General Anatomy in the Jefferson Medical College, Philadelphia, Pp. 1614; 1149 Engravings. Philadelphia and New York: Lea & Febiger, 1908.

THE semicentennial edition of any scientific work is worthy of comment for more reasons than one. As a general rule, books which belong to the "literature of knowledge" die with their authors, and in many cases are out of date even before that time; the perennial publication of new editions of works of the so-called "literature of power" calls for no special comment, for such classics never become superannuated. It must be, then, that *Gray's Anatomy* possesses certain peculiar characteristics which have not only caused it to survive its lamented author by nearly fifty years, but which have also made it almost impossible for its many rivals successfully to supplant it in the affections of teachers and students.

Comparing the first edition with the last, and with the fifteen intervening issues, one is struck forcibly by two things—first, that few of the original illustrations have been displaced; and, second, that the descriptive text has required scarcely any change other than amplification. Gray wrote his *Anatomy* in order to teach the subject to students; he set down in clear but graceful language the essential facts as they were then known; and he arranged his matter so skilfully as to render the appreciation of these facts easier when studied from his volume than from others then in existence. The facts themselves were not new, and equally accurate descriptions of the various parts of the human frame could be found in Sharpey, in Quain, and in other then popular text-books; but Gray's presentation of these old facts was new, and his illustrations were so far in advance of those in other works as at once to captivate the student's eye.

The previous American edition, also edited by DaCosta, was so favorably reviewed in these columns, and is so well known to the readers of these pages, that an extensive analysis of the present edition is not necessary. This new edition is more than twice the size of the original of 1858, and the number of the illustrations has been increased from 719 to 1149, mostly by the addition of figures from Spalteholz, Testut, Poirier and Charpy, and other European writers; but it is a notable commentary on the art of modern illustration to add that Gray's original woodcuts are still unsurpassed. The initial sections on general anatomy and on development have been omitted, as in the last edition; and the space thus gained has been used to expand and add to the paragraphs devoted to descriptive and surgical anatomy. In the new edition the surgical anatomy of the following subjects has been more fully developed: mastoid disease, the axilla, the cervical fascia, the prostate, the lymphatics and veins, and the abdominal organs.

The arrangement of the subject matter remains much as it was, with the exception of the chapter dealing with the central nervous system, which has been rewritten by Spitzka, about 100 pages being added to the matter contained in Pick's edition. It was probably necessary that this section should be rewritten, as so much new matter had to be added and so many new terms had to be introduced. It is, however, a matter of regret that the advance of knowledge and the changes in terminology render some paragraphs nearly unintelligible to graduates of more than a very few years' standing. We venture to assert, for instance, that none save neurologists or professed anatomists will appreciate at its true value the following description of the choroid fissure: "The rima is nevertheless a gap between the diencephalic part and the overlapping and recurved telencephalon produced by the extension of the secondary forebrain vesicle in an arcuate manner, which Hill described by the phrase 'rotation of the great forebrain.' It is along this arcuate and fissure-like gap that the richly vascular (pial) paraplexus invaginates the atrophied parietes of the secondary forebrain to form the paraplexus which is everywhere covered by endyma. The rima extends from the porta to near the tip of the mediacornu in an arcuate course and endymal reflections everywhere close in this gap except at the porta." Fortunately there are occasional oases in this desert of words in the nature of illustrations, which enable the student to see at a glance what it takes so long to describe. A number of the illustrations are from Dr. Spitzka's own pen; several of them show the deeper parts of the brain *in situ* as if seen through transparent overlying structures. "Special effort has been bestowed on combining the features visible to the naked eye with those seen only under high magnifying powers. By the knowledge of macroscopic and microscopic structures the attentive student is enabled to resolve or reconstruct, in the three dimensions of space, and see

with his mental eye the opaque interior resolved into intricate yet well-defined projecting and associating mechanisms."

Apart from the nervous system, the sections in which the greatest changes will be noted are those dealing with the lymphatics and veins. These are thoroughly abreast of the times; and numerous excellent illustrations have been added. In the edition of 1896 the lymphatics were discussed in thirteen pages, whereas in the present volume forty-two pages are devoted to the subject; while the section dealing with the veins has been expanded from thirty to more than fifty pages.

Some confusion seems to exist as to the relation of Colles' fascia to the base of the triangular ligament; in the text (p. 461) it is distinctly stated that the two layers of the triangular ligament are united to each other posteriorly, and that the superficial layer is continuous with Colles' fascia; yet illustrations from Denonvilliers, from Testut, from Henle, and from Poirier and Charpy (Figs. 308, 1062, 1052, 1048) are inserted which show the triangular ligament open posteriorly, and fibromuscular bands (the so-called recto-urethralis muscle) passing from the deep transversus perinei back to be inserted into the rectum; and the recto-urethralis muscle is spoken of in the text as equivalent to certain fibers of the pubococcygeus muscle (the *levator prostatae* of Santorini). It has been our own impression, from experience in the dissecting room, that the illustrations quoted are correct, and that the text is inaccurate, although the former editions of *Gray* described the triangular ligament in the same way.

The make-up of the volume is improved by the more generous use of heavy-faced type of various fonts, and by printing the origin and insertion of muscles in italics. The new international nomenclature has been introduced in parentheses after the classical names of the various structures. We regret to observe that the original dedication to Brodie, which disappeared first in the edition of 1905, is still missing.

It is safe to predict, on account of the familiarity of the profession with previous editions, that this new edition of *Gray* will continue to be welcomed as a household friend, and that teachers of anatomy all over the country will take an early opportunity to invite prospective members of the profession to join in the celebration of the golden wedding anniversary of *Gray's Anatomy* and students of medicine.

A. P. C. A.



AMERICAN PRACTICE OF SURGERY. Edited by JOSEPH D. BRYANT, M.D., LL.D., and ALBERT H. BUCK, M.D., of New York City. In eight volumes. Vol. IV; pp. 1010; 736 illustrations. New York: William Wood & Co., 1907.

THE successive volumes of the American Practice of Surgery continue to appear with commendable promptness. Volume IV concludes Part XIII, with a chapter on dislocations, by Emmet Rixford, M.D., of San Francisco. Part XIV comprises so-called operative surgery, embracing general considerations and the contra-indications to operating, by Charles B. G. de Nancrède, M.D.; preparations for an operation, by George Ben Johnston, M.D.; anesthetics and the production of general anesthesia, by Freeman Allen, M.D., and Frederick E. Garland, M.D., both of Boston; the production of local anesthesia for surgical purposes, by James F. Mitchell, M.D., of Washington, D. C.; amputations and disarticulations, by William Louis Rodman, M.D., LL.D., and John Stewart Rodman, M.D., of Philadelphia; excisions, by Horace J. Whitacre, M.D., of Cincinnati; ligature of arteries and veins in their continuity, by John M. Keyes, M.D., of New York City; minor surgery, by Russell S. Fowler, M.D., of Brooklyn; plastic surgery, by James S. Stone, M.D., of Boston; while the volume closes with Part XV, orthopedic surgery, including articles on congenital dislocations, and infantile paralysis, both by Charles F. Painter, M.D., of Boston; torticollis, by George D. Stewart, M.D., of New York City; deformities and disabilities of the lower extremities, by Royal Whitman, M.D.; and tuberculous disease of the spinal column, by Clarence L. Starr, M.B., M.D., of Toronto.

Dr. Rixford covers the subject of dislocations in a fairly satisfactory manner, especially interesting being his descriptions of the mechanism by which the various luxations are produced. Probably no two surgeons will ever be in entire accord on this perplexing topic; but we had thought the idea that the humerus is dislocated "in a considerable proportion of cases," by blows on the point of the shoulder, had long since been abandoned; nor can we be persuaded that the theory of "transmitted thrust" will satisfactorily account for dislocation of either end of the clavicle. It seems much more reasonable to invoke here, as at the elbow and the hip, the theory of leverage. In speaking of "Kocher's method" of reducing luxations of the shoulder, Rixford states that it is a modification of Schinzinger's; but he fails to credit Henry H. Smith, formerly professor of surgery in the University of Pennsylvania, with being the first to systematize the reduction of shoulder dislocations by manipulation, and teaching to his students a method closely resembling Kocher's long before the name of Kocher was known in surgery. It is worthy of note, perhaps, that among 28 cases treated by Kocher himself by his own method of manipulative reduction, he produced

three fractures of the humerus. It is a pleasure, on the other hand, to see the credit given Allis for his monumental work in connection with dislocations of the hip. In attempting to explain the classification and nomenclature of dislocations of the ankle, we cannot but think that Dr. Rixford resembles that ancient personage referred to in the Bible as darkening counsel by words without knowledge.

In discussing the preparations for an operation, Dr. Johnston seems a little too prone to think only of abdominal surgery. He advises the routine administration of morphine  $\frac{1}{4}$  to  $\frac{1}{2}$  grain, with atropine  $\frac{1}{100}$  to  $\frac{1}{50}$  grain before operation. That the combined cap, face-mask, and hood, for operating, covering everything from the vertex to below the shoulders, is especially valuable in hot weather, is a dictum to which many surgeons will not accede. Dr. Johnston considers that "all disinfectants, except soap, are unnecessary." This is one among several quasi-epigrammatic statements made in the article which seem injudicious, even if literally true.

Under local anesthesia, Mitchell discusses also spinal anesthesia. The latter he prefers to strictly local anesthesia only in rectal and prostatic work.

Amputations and disarticulations are described in a rather perfunctory manner, and there is occasionally a little carelessness of expression which is distressing. There is no mention of the proper relation of flaps formed by transfixion to the vascular supply of the limb; and were surgeons to follow the directions given there would be great danger of the point of the knife slitting up the femoral artery in Hunter's canal, or the brachial in the middle of the arm. Moreover, we fail to see why grasping the amputating knife between the thumb and forefinger of the right hand is especially important if the operator stands to the left of the patient (p. 275)—unless, perchance, the authors aim to inculcate ambidexterity; and prefer to use the "thumb and forefinger" of the left hand when standing on the patient's right. At best, it must be admitted that a somewhat insecure grasp is afforded by the "thumb and forefinger" of either hand. The long anatomical descriptions might well have been omitted. Twenty-three pages (out of a total of 104) are devoted to amputations of the foot. The space gained by curtailing these sections could have been devoted with profit, we believe, to the indications for the special methods of amputation, a subject which is too little appreciated by the average surgeon, and one which Dr. Rodman from his wide experience, should be well fitted to teach. A few paragraphs on the adaptation of artificial limbs have been added, but in a work which aims to be abreast of the times it is strange that the work of Vanghetti and of Ceci in performing amputations suitable for cinematic prosthesis is not even mentioned. Original illustrations are conspicuous by their scarcity.

There is nothing particularly noteworthy in Dr. Whitacre's

account of excisions. He states that there is a tendency for surgeons to be more radical in their operations for tuberculous bone disease; this statement scarcely seems to be warranted at a time when hygienic surroundings and open-air treatment of such patients are surely steadily decreasing the number of operations required. He flatly contradicts himself (pp. 427 to 434) as to the indications for excision of the hip in ankylosis. He waxes quite enthusiastic over formal excisions of the wrist and ankle, operations on which most surgeons of experience have placed a ban.

One might expect to find in the article on ligature of arteries and veins some reference to arteriorrhaphy; but even the suture of veins is not mentioned. It is to be hoped that these topics of actual interest will find a place somewhere among the eight volumes.

Plastic surgery is treated in a lengthy and cyclopedic monograph by Stone. Following an excellent account of the principles of plastic surgery, the various special procedures are described, and amply illustrated. He is very cautious in his recommendation of paraffin prosthesis, dwelling upon the immediate dangers and the remote failures.

Painter contributes a pessimistic article on congenital dislocations. He accepts foetal malformation as the cause. He thinks true congenital luxation of the shoulder very rare, believing this deformity when found in infancy to be usually due to obstetrical or infantile palsy. He classes Madelung's disease with congenital dislocation of the wrist, believing it to be acquired before birth, but that its manifestations are delayed until the age of puberty. In the account of the history of congenital luxation of the hip, the name of Paci is not even mentioned, although Hoffa and Lorenz are given prominent places. He states that all cases cannot be treated successfully by identical means, an important truth which is sometimes forgotten; and before deciding on the method of treatment, he thinks the surgeon should determine the anatomical condition of the head and acetabulum, and the relation of the former to the shaft. He states that when reduction has been accomplished the occurrence of relaxation during application of the cast ought not to be easy if permanent success is to be attained. He uses the Bartlett or Bradford machine for reduction; he regards the production of hematomas and tears of the skin as "not often of serious consequence," acknowledges to having himself fractured both pubic rami by the machine, and speaks lightly of other accidents, the most serious being rupture of vessels, fracture of the femur and pelvis, and occasional injury of the great trunks. Surely those who wish surgery to be a gentle art will have their hair made "to stand on end like quills upon the fretful porcupine" when they read these paragraphs.

In reviewing the third volume of the *American Practice of Surgery*, we noted with regret that the subject of Pott's disease of the spine had not been assigned to Prof. Primrose; but we count the sub-

scribers to these volumes fortunate in that it is treated in the present volume by a colleague of Primrose. Dr. Starr presents his readers with a most admirable article—indeed, the best in the volume—which sets forth in a lucid and scholarly manner the pathology, symptomatology, and treatment of this serious disease and its complications. Among the latter is abscess, which is considered responsible for the great bulk of deaths, either from prolonged suppuration, or from the development of tuberculous meningitis. Infection with organisms other than the tubercle bacillus, he holds, may arise in three ways: (1) Usually from the sinus through which the abscess discharges; (2) not infrequently from the deeper layers of the skin (sweat and sebaceous glands) as the abscess approaches the surface; and (3) through the blood current. The great problem, therefore, is to prevent the discharge of the abscess or its infection by “pyogenic” organisms. He quotes Calot’s aphorism that the spontaneous opening of an abscess is “an open door through which death very quickly enters.” He advocates, therefore, early free incision of the cold abscess, as soon as it approaches near enough to the surface to be accessible, but before the skin itself has been invaded by tuberculous disease. This is followed by thorough evacuation of its contents, wiping its walls dry with iodoform gauze, and suturing the incision tight by deep sutures. Among 60 cases which he has treated in this manner, 51 have remained perfectly closed for periods varying from six months to five years. When this is compared with Primrose’s experience, narrated in Vol. III, we think the value of this method over that of repeated (and usually unsuccessful) aspiration and injection, or waiting for the spontaneous evacuation of the abscess, has been sufficiently demonstrated.

A. P. C. A.

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#### DISEASES OF THE GENITO-URINARY ORGANS AND THE KIDNEYS.

By ROBERT HOLMES GREENE, A.M., M.D., Professor of Genito-urinary Surgery in the Fordham University, New York, and HARLOW BROOKS, M.D., Assistant Professor of Pathology in the University and Bellevue Hospital Medical School, New York. Pp. 536; 292 illustrations. Philadelphia and London: W. B. Saunders Co., 1907.

THIS book is a conjoint product of a surgeon and a physician, and the subjects are considered from the standpoint of the general practitioner and the surgeon. After carefully perusing the work, we believe that it will be of more value to the former than to the latter.

It presents all the latest improvements in the diagnosis of the diseases of the genito-urinary tract. The chapter on cystoscopy

shows well the knowledge that can be obtained of vesicorenal conditions by this instrument in experienced hands. The directions for its use are given in detail. The medical aspects of Bright's disease, together with the application of surgery to the treatment of this condition, are set forth in full. The chapter on tuberculosis of the kidney presents many admirable points, but is open to some criticism. In the first place, insufficient stress is laid on hematuria, and how it can be differentiated from the hematuria occurring in other conditions. No mention is made of the danger of infecting the normal kidney by catheterization of the ureters when the bladder itself is a seat of a tuberculous lesion. No mention is made under the head of kidney or bladder tuberculosis of the good results obtained by early nephrectomy.

As has been indicated before, the portions of the book dealing with operative technique are most open to criticism. For instance, in operating for calculus, needling of the kidney is recommended for localizing the calculus. Any surgeon with experience knows how unreliable this measure is.

Considerable attention is given to the subject of floating kidney, but not sufficient to the mechanical support of such a kidney by a properly fitting corset. In the diagnosis of this condition the passage of metal ureteral catheters, which may indicate the position of the kidney in an x-ray plate, is recommended. Such a diagnostic measure in the hands of any but the most experienced must be a dangerous procedure in the presence of a diseased or kinked ureter. In describing the operations for fixation of the kidney, no mention is made of that operation which was first suggested by Harris, of Chicago, which has for its object the obliteration of the peritoneal pouch, into which the kidney falls. Again, illustrating the deficiency of the work as a guide for the operative surgeon, we quote the following paragraph, which is all that is given on the operation of ureterotomy for stone, excepting a brief mention of the extra-peritoneal operation: "For removing a stone from the ureter, the longitudinal incision is the preferable one. Occasionally, operating through the bladder, a stone may be removed from the ureter by the finger or by the use of long narrow forceps if the mouth is, as occasionally happens, dilated." It will be observed that no mention is made of suturing the ureter, or whether or not drainage is indicated, two important points in the operative technique.

The chapter on stone in the bladder is good, and the closing portions of the book, which deal with lesions and deformities of the external genitalia, are up-to-date and authoritative. J. H. G.

**THE BACTERIOLOGY OF DIPHTHERIA, INCLUDING SECTIONS ON THE HISTORY, EPIDEMIOLOGY, AND PATHOLOGY OF THE DISEASE, THE MORTALITY CAUSED BY IT, THE TOXINS AND ANTITOXINS, AND THE SERUM DISEASE.** By F. LOEFFLER, M.D., LL.D.; AURTHUR NEWSHOLME, M.D., F.R.C.P.; F. B. MALLORY, M.A., M.D.; WILLIAM H. PARK, M.D., AND CHARLES F. BOLDUAN, M.D. Edited by G. H. F. NUTTALL, M.D., PH.D., Sc.D., F.R.S., Quick Professor of Biology in the University of Cambridge, Fellow of Christ's College; and C. S. GRAHM-SMITH, M.A., M.D., University-Lecturer in Hygiene, Cambridge. Cambridge at the University Press, 1908.

THIS book is truly a monumental work upon the bacteriology of diphtheria. From every point of view the subject is discussed exhaustively. In such extensive treatises, in which the various sections are written by different persons, it not infrequently happens that there is a good deal of repetition, but owing to the excellence of the editing of this book such an error has fortunately been avoided. The book opens with an introductory chapter on the history of diphtheria, contributed very appropriately by Loeffler; an interesting section then follows by Newsholme on the epidemiology. Mallory contributes a splendid section upon the pathology of diphtheria, fully illustrated by reproductions of photo-micrographs. The text is based principally upon the study of 251 cases of diphtheria which came to autopsy at the Boston City Hospital. The section upon diphtheria bacilli and diphtheria-like bacilli, containing several chapters and covering over 300 pages, is written by Graham-Smith. The subject is considered in the greatest detail and the various chapters contain practically everything that is known about this group of organisms. In regard to the relationship between the true diphtheria bacillus and the pseudo-diphtheria bacillus, or *Bacillus Hofmanni* as Graham-Smith terms it, he states that there is no evidence to show that the one is an attenuated and non-pathogenic form of the other; he thinks, rather, that the recent investigations go to show that the two organisms belong to different species. In one chapter he has collected interesting statistics bearing upon the presence of virulent and non-virulent diphtheria bacilli in the throats of healthy persons. From the study of between 2000 and 3000 reported cases he finds that virulent diphtheria bacilli are found in the throats of 0.1 to 0.2 per cent. of healthy persons, whereas non-virulent bacilli are found in from 1 to 2 per cent. On the other hand, a large proportion of persons who actually come in contact with cases of diphtheria, harbor virulent bacilli in their mouths, 8.7 to 66 per cent. In the chapter upon modes of infection he points out the possibility, though slight, of milk epidemics. One chapter in the section by Dean on the types

of immunity and the toxin of the diphtheria bacillus, is devoted to a discussion on the effects of antitoxin on toxin, and is given over in large part to a criticism of the views of Arrhenius and Madsen. The book closes with two chapters by Park and Bolduan, one on the mortality of diphtheria, and the other on the serum sickness. The book which numbers 700 pages is probably the most complete treatise upon the bacteriology of diphtheria that has ever been written, and as a book of reference is invaluable. The bibliography at the end of the volume covers over 60 pages.

W. T. L.

CLIMATE, CONSIDERED ESPECIALLY IN RELATION TO MAN. BY ROBERT DECOURCEY WARD, Assistant Professor of Climatology in Harvard University. Pp. 374 illustrations. New York: G. P. Putnam's Sons; London: John Murray, 1908.

IN spite of the author's reassurance that *Climate* is intended to be "a book which can be read by any intelligent person who has not had special or extended training in the technicalities of the science," the first part of the book is nevertheless somewhat difficult for the uninitiated to follow. The first impression produced is that a very large amount of material has been compressed into a very small compass, and to the lay reader it seems that many things are either left to his imagination or taken for granted as matters of common knowledge. The book could be greatly expanded without adding any new material, and the numerous examples taken from almost every branch of knowledge call for more liberal treatment.

Passing over the initial chapters devoted to technical matters, such as nomenclature, classification, and the like, we come to a wealth of interesting statistical information in the chapters on the characteristics of the zones, dealing with such questions as the physiological effects of heat and humidity, the effects of season and weather on man, and marine and mountain climates. The effects of climate on man, his customs, manners, pursuits, and lines of development, are interestingly set forth in separate chapters under the three general subdivisions of tropical, temperate, and polar zones. The author points out, however, that other factors must be considered in explaining many of the phenomena that have been rashly attributed to the influence of climate alone; such as the color of man's skin, which is believed to become paler with increasing distance from the equator; the overhanging eyebrows and partly closed eyes of the negro; the small stature of the African pygmies, which has been attributed to the heavy equatorial rains. Migration from place to place, with the accompanying change in man's food, habits, and pursuits; heredity; intermarriage; the character of the soil and

the different opportunities it creates, and, finally, the element of time are some of the factors that, no less than climate in the narrower sense, contribute to the final result whatever it may be.

In the chapter on the hygiene of the zones the author adopts, to a certain extent, the medical standpoint and in his medical facts he is quite accurate. The important part played by microorganisms in the production of disease is fully appreciated. The beneficial effects of different climates and the reasons therefore are interestingly discussed—the stimulating effect on the breathing apparatus of the rarefied air of high altitudes; the purity and freedom from germs of desert air, without the stimulating qualities of mountain climates, which are sometimes undesirable; the beneficial effects of forested areas in pulmonary tuberculosis; the purity, freedom from dust, and equability of temperature of ocean air so beneficial during convalescence; the ventilating and putrifying action of the winds in congested districts; the germicidal action of sunlight and the interference with this action by fogs and clouds. The geographical distribution of diseases is, however, by no means definite, being subject to many exceptions and variations. Seasonal differences are often due to some secondary factor, such as overcrowding under unhygienic conditions during the winter season. We commend particularly the paragraphs devoted to individual diseases and their distribution. Much light has been shed on this interesting subject by recent discoveries, notably in regard to tropical diseases. It is pointed out that it is not so much the climate that produces or favors a certain disease, as the fact that conditions in certain localities are favorable to the life of the cause of the disease, as in the case of malaria and yellow fever and all diseases dependent directly or indirectly on animal life.

R. W. G.

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OUTLINES OF PSYCHIATRY. By WM. A. WHITE, M.D. New York: The Journal of Nervous and Mental Disease Publishing Co., 1907.

THIS small volume of two hundred and thirty pages, by the superintendent of the Government Hospital for the Insane, Washington, D. C., is the first of a series of monographs on nervous and mental diseases. The editors, Drs. Jelliffe and White, announce that the series will consist of short monographs, translations, and minor text-books on subjects related to nervous and mental diseases. The publication of this work will, therefore, establish a new departure in the literature of nervous diseases and psychiatry, and it is to be hoped will lead to a more systematized presentation of investigating work in this field. The need for the opportunity of



presentation of work in such a form has long been felt, and, with proper care and selection of the work presented there need be no question as to the success of the project.

Dr. White's work on psychiatry is a systematic presentation of mental diseases. The first half of the book is devoted to general considerations, with a very full and important chapter on the examination of the insane (in the preface the author expresses his indebtedness for this chapter to Dr. Shepherd Ivory Franz). This portion of the work is presented with a thoroughness and scientific insight that is somewhat lacking in the detailed presentation of the individual psychoses in the second half of the volume. This, however, is evidently not a matter of ability on the part of the author, but is evidently due to the lack of space for the presentation of his subject. It is simply impossible to present in one hundred and twenty pages a description of the various types of mental disease in such a way that each will stand out as a clear-cut picture in the mind of the student or practitioner who has only an occasional opportunity to see mental disease. It will, on the other hand, suffice for an outline for those who have an opportunity of studying large numbers of cases. For those, indeed, it will have a special value, in teaching them the use of the technical language so necessary to describe mental states. That this was evidently the purpose of the author is indicated by printing the technical expressions in italics.

The grouping of the different mental states follows that in a general way advocated by the German schools, and is probably the most used for the purpose. It is, however, questionable whether the consideration of the various mental diseases of adolescence, which have been grouped under dementia precox, is scientifically or clinically correct. This tendency has led to the inclusion of certain mental states, more particularly under the paranoiac group, which had better be treated separately. For this reason a consideration of all these cases of dementia precox as abiotic forms of disease is decidedly open to question.

The pathology of the different forms of mental disease is carefully considered as far as the limited space permits. The statement, however, that the disappearance of the tangential fibers accounts, in a measure, for the dementia of the senile psychoses, is too sweeping a statement, and probably incorrect. In the atrophic processes seen in such a wasting disease as tuberculosis, the disappearance of the tangential fibers is not associated with any distinct dementia.

One cannot help feel that, while the publication of Dr. White's work will add to the value, and especially to the success, of the monograph series, it would be better if this work had been published in a more extended and stable form. It is to be hoped that we may have in the future a more extensive work upon the same subject and along the same lines by this author. The work is published on poor paper and in a paper binding. It is worthy of a more stable structure.

D. J. McC.

**PRACTICAL ANESTHETICS.** By H. EDMUND G. BOYLE, M.R.C.S., L.R.C.P., Assistant Anesthetist to St. Bartholomew's Hospital, London. Pp. 178; 22 illustrations. London: Henry Frowde, Oxford University Press; Hodder & Stoughton, 1907.

THERE should be cordial welcome for any book which attempts to instill into the minds of students and junior hospital internes some of the principles underlying the use and administration of anesthetics, before they are in a position to make practical application of their ignorance of these principles. The manual now before us opens with a chapter on "general considerations," in which are discussed the duties of the anesthetist, examination and preparation of the patient; apparatus required; position of the patient; moving of the patient; and the after-treatment, as well as the subjects of shock, collapse, and artificial respiration. There follow chapters on nitrous oxide, on ether, on chloroform, and on ethyl chloride. The concluding chapters discuss the subject of mixtures and sequences of the various anesthetic substances; the question of the selection of the anesthetic for various operations; and the administration of the anesthetic with the patient in different positions—prone, lateral, high-pelvic, sitting, etc. Neither spinal nor local anesthesia is considered.

Nitrous oxide is recognized as the safest; and ether is in general preferred to chloroform. As Mr. Boyle tersely puts it, it is better that "patients should suffer from bronchitis after ether than that they should die on the table from chloroform." He thinks the safety of ethyl chloride has been exaggerated, and believes its dangers should be rated as equal to those of chloroform, because of the rapidity of its action and the liability to spasm. He prefers to induce anesthesia with nitrous oxide gas and oxygen, and maintain it with ether; if the operation is to be prolonged, he changes to chloroform after fifteen or twenty minutes. He advises the "closed" method of administering ether, condemning the "open" method so much used in this country in the following words: "The open method is only adaptable to children or to much exhausted patients. An attempt to anesthetize a robust patient by means of ether poured on lint would result in the formation of much snow on the lint, the using up of several half-pint bottles of ether, and would terminate in failure." Whether climate can make such a difference, we know not, but certainly no such difficulties attend the "open" administration of ether in this country; two ounces of ether has usually been sufficient in our own experience to induce anesthesia, and it usually can be maintained at the rate of about six ounces an hour, should the operation last so long.

A. P. C. A.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**The Gastric Secretion in Old Age.**—JULIUS FRIEDENWALD (*Amer. Med.*, 1908, xiv, 275) notes that most of the previous work of gastric secretion has been done with young adults. However, later work has shown and some authors have pointed out the occurrence of atrophic changes in the stomach as well as the disappearance of free HCl. This hypochlorhydria is supposed to be related to and proportionate to the degree of arteriosclerosis. After a review of the literature of the subject Friedenwald gives his observation in 27 persons, all over fifty-five years of age and none having symptoms of gastric disorder. Free HCl was constantly absent in 44 per cent., and in only 5 of the 27 was there a normal percentage of free HCl. In 18 of the patients who had arteriosclerosis, 10 showed an absence of free HCl, and the remaining 8 much diminution. Friedenwald concludes from his own observations, as well as those from the literature, that the gastric secretion has a tendency to diminish in old age and in a degree proportionate to the arteriosclerosis. It is, therefore, unwise to attach too much importance to the absence of this secretion in individuals advanced in years in the diagnosis of cancer of the stomach.

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**Tuberculin Inunction.**—ERNST MORO (Munich) (*New York Med. Jour.*, 1908, lxxxvii, 1233) suggests a new tuberculin reaction by rubbing into the skin of the chest or abdomen an ointment made up of Koch's old tuberculin, 5 c.c., and anhydrous wool fat, 5 grams. A piece the size of a pea should be rubbed over an area of the skin about two inches square for about half a minute and allowed to become absorbed. Observation, which is usually best on the second day, reveals the presence of small papules over the area of inunction or thereabouts if the reaction is positive, and no change in the skin if

negative. The papules may be very pale and scarce, but occasionally are numerous and red. Exceptionally there is very much redness or itching. No local or general symptoms have been observed. The papules usually disappear at the end of a week. Moro says a positive result is as conclusive as that of the conjunctival or skin reactions. The only difference noted is that in advanced cases of tuberculosis the skin loses early its reactionary power to the inunction. In other cases that show no clinical signs of tuberculosis the percentage of positive results is much smaller in the inunction method. Another advantage of this method is that the applications are harmless when compared to the other reactions (the skin and eye), and the patients do not object to its use.

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**Continuous Inhalation of Oxygen in Pneumonia.**—GEORGE STOKER (*Medical Press and Circular*, 1908, lxxxvi, 90) notes that oxygen when used late in the disease, when the patient is cyanotic and gradually sinking, is often useless, giving but temporary relief. He thinks that it is this delay that has brought discredit on oxygen as a therapeutic agent. For the continuous effective inhalation it is essential to use a gas bag holding one cubic foot of oxygen filled and refilled from the cylinder as needed. This prevents gas from being inhaled when too cold and also measures the exact amount of gas which may be given in a certain length of time. It requires usually about two hours to empty the bag when under slight pressure. A soft rubber nose piece should be used and its tip inserted into one or the other nostril, as when held before the patient's mouth in the usual method it is found useless. Stoker reports at length a case of pneumonia treated in this manner as outlined above, in which all the symptoms subsided and the patient made a complete recovery within nine days. He concludes that the best results will be obtained when the oxygen is given as soon as the disease declares itself, and that the inhalations must be continuous day and night and kept up as long as the symptoms persist.

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**Treatment of Gonococcic Arthritis by Injections of Dead Gonococci and the Clinical Reaction which follows the Injections.**—E. E. IRONS (*Arch. Int. Med.*, 1908, i, 4333) gives the result of 40 cases of gonococcic infection inoculated with varying doses of the organisms, and concludes that in certain chronic cases the mechanism of immunity fails to rid the body of the organisms and they persist either in the original lesions or in one or more foci, thus giving rise to the new lesions in these cases. The injections seem to be of distinct value in these cases and of no harm. The dosage was at first 20,000,000 to 50,000,000 organisms, but later it was found advisable to increase to 100,000,000 and more. The interval between the injections varied from three to seven days. Further work and reports will enable one to give a more accurate dosage, and the percentage of favorable results, it may be hoped, will be greater. During the course of the injections the usual general therapeutic measures should also be tried. As a diagnostic procedure it may be of more use, as the reaction has many points in common with the tuberculin reaction; it should prove to be reliable (it must be tried in many more cases), and a valuable and much needed aid will be at hand for the diagnosis of obscure joint, synovial, and periosteal disease.

## SURGERY.

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**Radical Operation for Umbilical Hernia by Overlapping of the Flaps.**—**BRENNER** (*Archiv f. klin. Chir.*, 1908, lxxxvi, 20) says that since Lawson Tait, in 1884, first proposed this operation, there have been a large number of them done, although they are not all reliable; and the proportion of operations done to the total number of cases is small and the recurrences still too frequent. Pott, in 1903, estimated the permanent cures from operation for inguinal herniæ to be 92 per cent., in femoral 92.5 per cent., and in umbilical 54.7 per cent. for all methods. His collected cases from the literature show 4066 inguinal herniæ, 424 femoral, and 86 umbilical. Brenner found about the same proportions in a collection of hospital cases operated on. The results of operation in umbilical herniæ depend in large measure upon the size of the hernia. Busse in the small herniæ (from the size of the hazelnut to that of a walnut) obtained 100 per cent. of permanent cures, in the medium sized (apple to a goose egg) 50 per cent., and in the largest (double fist to a man's head) 25 per cent. The average permanent results should be estimated from the large and median sized herniæ, in establishing the value of radical operation. The various methods of operation are discussed. The method which Brenner has employed is very similar to and probably identical with that published by Wreden in 1906, but which Brenner had done in 4 cases before that time. He has already employed it in 26 cases up to the present time, 19 umbilical, 3 epigastric, and 4 ventral. Lumbar anesthesia is preferred. A sagittal incision is made over the hernia, and in the upper part, where the covering is thin, an elliptical portion is removed. The sac is isolated, opened, and the contents properly examined and returned. The sac is removed and the hernial ring closed by several sutures which include the peritoneum and the aponeurosis. The mass of fat covering the aponeurosis between the edges of the recti is then removed. The inner borders of the recti are then carefully exposed through small incisions in their sheaths. They are often 10 to 15 cm. apart, and their separation narrows below to the symphysis and above to the costal arch. This elliptical field must be strengthened and the umbilical ring obstructed by the two flaps which are to be made from the anterior sheaths of the recti. The fat is first lifted from the aponeurosis over the recti in a curved field, convex outward, far enough so that a flap of aponeurosis can be lifted from over each rectus, its cut edge being external and its attached border internal. This semilunar flap must be large enough, so that

when it is separated by an arching incision along the outer margin of the exposed area and the flap is turned over toward the median line, it will reach to the inner border of the rectus of the opposite side. When both flaps are formed, the left one is turned over and its cut edge sutured to the inner attached border of the right flap, which is in turn inverted over the left. The elliptical area interposed between the separated recti is thus reinforced by these two new layers and the recti muscles are visible in their denuded areas. The skin flaps are then closed by sutures and drainage provided. In one case the wound was opened eight days after operation, and the flaps showed good nourishment. In another case from fat necrosis the edges of the wound separated, showing one of the flaps, which gradually became covered by granulations. Skin grafting was later performed and a permanent cure obtained. Of the 26 cases operated on, 3 died; 1 eight days after operation from a hemorrhage of a duodenal ulcer; a second three days after operation from necrosis of the transverse colon due to disturbance of the blood supply during the separation of the hernial ring; and a third case from septic peritonitis. The average course of the wound healing in the remaining 23 cases, was twenty-eight days.

**Pulmonary Emboli after the Radical Cure of Inguinal Hernia.**—MAUCLAIRE (*Archiv. gén. d. chir.*, 1908, ii, 573) says that the discussion of postoperative emboli has concerned itself chiefly with its origin in appendicitis. Pulmonary emboli have been reported as occurring in cases of strangulated hernia, and Mauclaire thinks that the emboli reach the systemic circulation, probably, through the anastomoses between the portal system and the inferior cava. Following the simple radical operation for inguinal hernia, they are rare enough to warrant the report of additional cases. Fifty cases from the literature are studied and one personal case reported. The etiology is the most interesting feature of the subject. The causes are divided into local and general. The local include the local infections; and lesions of the epigastric vessels, femoral vein, and spermatic vessels. The general include general infections, the condition of the blood and heart, the condition of the local veins or those of the rest of the body, and too early standing after operation. Local infections require first consideration. It has been shown to have been present in several cases. Some authors found the wound normal, but suspected the deeper parts. In Mauclaire's case it was evident that the embolus resulted from a phlebitis of the spermatic cord in consequence of the manipulations during the operation. It may be transferred to the opposite side by anastomotic veins. This phlebitis has been observed in cases of gonorrhoea and varicocele. Bruner observed it in 50 cases. In 400 or 500 radical operations done by Mauclaire in the past ten years, it was observed four or five times. It can be complicated by early or late emboli. The femoral vein may become involved in the course of the operation or the later dressings. The phlebitis develops sometimes on the side corresponding to the operation, sometimes on the opposite side, just as it does from appendicitis. In cases of femoral phlebitis consecutive to operation for inguinal hernia, the lesion of the epigastric vein may be the original cause, the phlebitis extending to the femoral vein. By the anastomoses between the epigastric vein of the two sides or by the obturator veins, extension

may occur to the opposite side. Pulmonary embolus in these cases is often fatal. The palliative treatment consists in avoiding or treating the local or general causes.

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**The Treatment of Acute and Subacute Suppurations by Bier's Passive Hyperemia.**—HEINRICHSEN (*Archiv. f. klin. Chir.*, 1908, lxxxvi, 158) says that his first results from this treatment led him to be skeptical of its value. These results were dependent partly upon a faulty technique, and partly upon cases unfavorable for the method. The constricting bandage should be applied either to the arm or thigh. The turns should not completely cover each other, but should surround the greater part of the limb, and the position should be changed somewhat at each application, if possible. The rubber bandage was protected underneath by a thin cotton bandage on the thigh, but on the arm no such protection was employed. Care, however, was observed not to permit wrinkling of the bandage, which might cause the formation of blisters. The passive hyperemia was continued twenty to twenty-two hours daily in acute cases, and ten to twelve hours in the subacute. For the shoulder-joint it was kept up only ten hours. Around the neck, a bandage 2 to 3 cm. broad was employed. Cupping apparatus was applied forty-five minutes to one hour. It may be applied for five minutes, then removed for two to three minutes, and re-applied for five minutes. In all, 178 cases were treated, 103 only by cupping, 71 by bandage, and 4 by a combination of both. The results showed that, under certain conditions, passive hyperemia in acute inflammations gives good results in a shorter time, and is to be preferred to a wide incision. To avoid failure the hyperemia must be given in proper dosage, the patients must be under continual observation and the wound not tamponed. The temperature after this treatment usually falls by crisis, rarely by lysis. In many instances there will be no inclination of the temperature to fall, but this is not an indication for a wide incision. Good results are obtained in cases of recent wounds and operations, in which infection is suspected.

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**Osteoplastic Filling of the Defect after Resection of the Lower Jaw with a Piece of Rib by Means of a Pedicle Flap from the Chest, or by a Free Transplantation.**—PAYR (*Zentralbl. f. Chir.*, 1908, xxv, 1065) has for some years been filling the defect by different kinds of prosthetic apparatus, made of magnesium. This consisted either of a splint made of magnesium plate, or a strong magnesium wire. These were suitably bent and introduced into holes made in the ends of the resection stumps, or, if a resection had been done on one side, the apparatus was attached by holes on the surface of the articular tubercle. He says that he would employ now such an apparatus carrying a metal head corresponding to the glenoid cavity. For the substitution of a resected middle piece of the jaw he advises a splint made of magnesium wire with two clasps attached to its ends, which are to be fastened by wire or screws, placed in holes bored in the resection stumps. This apparatus is applied easily, keeps the bones in good position, requires small space, and favors an exact closure of the cavity of the mouth. In one such case, in which the wire was employed, in ten days a complete water tight protection of the wound from the mouth was obtained. The plate has the

disadvantage that its sharp margins produce a secondary necrosis of the mucous membrane by pressure. In most of the cases the wire was removed in from seven to ten weeks, and was replaced by a dental substitute. In one case the magnesium apparatus healed in without a fistula, and was completely absorbed and replaced by a thick and cosmetically sufficient scar. Only isolated attempts have been made to fill the defects by osteoplastic methods. No appropriate osteoplastic method has yet been developed for the different requirements, and brought into general use. Payr, for several years, has been considering the advisability of employing a piece of rib covered by periosteum for this purpose. This may be accomplished in one of two ways. A piece of rib of suitable length may be resected through a small incision below the clavicle, and then displaced between the skin and fascia to a new position, from which the skin and fascial flap is to be taken later. The concavity of the resected piece is made to look toward the skin. After two or three weeks, a new vascular supply is established between the piece of rib and the surrounding tissues. In the second operation the diseased portion of the jaw is removed and is replaced by the rib carried in a long, wide, tongue-shaped flap of skin and fascia, the piece of rib being fastened into the defect in the jaw. Finally, the skin flap is employed to fill in defects in the mucous membrane or skin, or it is replaced in its original position. A second method is by the free transplantation of a piece of rib into the defect. Payr has employed the first method in 2 cases and the second in 1, with good results.

**The Pathology of Cholelithiasis.**—EXNER and HEYROSKI (*Archiv f. klin. Chir.*, 1908, lxxxvi, 609) say that bacteria in the bile, by their growth, decompose glycocholate and taurocholate of sodium, as well as other biliary salts. Then the cholesterin is not held in solution, because of the absence of these salts. Some bacteria are especially capable of producing this decomposition, and are therefore especially prone to give origin to stone formation. Even in bile sterile for a long time decomposition of the biliary salts can occur. The soap and fat contained in the bile play no part in the development of cholesterin. The bodies in the bile, considered up to the present time to be fatty acids, actually contain only a small proportion of fatty acids. The proportion of these acids in the bile is actually, approximately, only one-tenth of what it has been supposed to be. These facts are of much importance in connection with the origin of gallstones, since they show that bacterial infection of the gall-bladder must result in cholesterin formation and thus give cause for the formation of cholesterin calculi.

**The Development of Weight-bearing Stumps, by Means of Hirsch's After-treatment, in the Japan-Russian War.**—HASHIMOTO and SAITO (*Archiv f. klin. Chir.*, 1908, lxxxvi, 589) report the results of amputation of the lower extremity in 38 cases, in some on both sides of the body. The after-treatment consisted in elevation of the limb, massage several times daily, wrapping the limb in cotton after the massage, treadng exercises, a lysol bath every evening, standing several times daily upon a provisional apparatus the cavity of which was filled with cotton, and walking exercises upon this apparatus. Amputation is one of the most important operations in military surgery. Upon the battle



field, every aid should be provided, in order to avoid crowding of the wounded men. All efforts must be made to transport the wounded, the wound put in as favorable a condition as possible, so that infection and hemorrhage in transport shall be avoided. Hashimoto and Saito recommended a quick and simple amputation on the field of battle, by the circular incision through the bone or joint. The stump will not be at once weight-bearing. The osteoplastic operations, having for their object an early weight-bearing stump, are too troublesome or dangerous for employment on the battlefield. When a rapid amputation is necessary as on the battlefield, the circular method with the Hirsch after-treatment, is recommended. This gave good results in their 38 cases. When time during the operation is not a factor, and a choice can be made of a method which will give undisturbed wound healing, then the stump should be selected which will soonest bear weight.

**Tetany following Thyroidectomy Cured by the Subcutaneous Injection of Parathyroid Emulsion.**—BRANHAM (*Annals of Surgery*, 1908, xlviii, 161) reports a case in which a goitre was removed from a girl, aged fourteen years. Although an effort was made to avoid the parathyroids, it was afterward shown that some parts were removed with the gland, some remaining. The patient was apparently making an uninterrupted recovery, until eighty-eight hours after the operation, when the teeth became clinched. Shortly afterward the hands became contracted and the feet affected (talipes equinovarus), wrists flexed on the forearms (full flexion) and the forearms slightly flexed on the arms (at right angles). Reflexes were not exaggerated, no elbow or wrist jerk. The head was thrown back, teeth clinched, but the face not distorted. Only her head, shoulders, buttocks, and heels touched the bed. The temperature was 38.5° C., and the symptoms toward the last of the attack were alarming. There were distinct exacerbations like those of tetanus, during which the pulse was rapid and the respirations difficult. Thyroid extract in doses of 0.192 gram were ordered every three hours, and every four hours she was given 0.0648 gram of parathyroid extract. No relief followed, but the contractions became more marked. On the following day, six raw, fresh beef parathyroids were forced into the mouth and they were swallowed. This was repeated on the next morning and night. The symptoms became more pronounced. On the same night, five of the glands were placed in a 1 to 1000 bichloride solution and allowed to soak ten minutes. Observing strict asepsis, the glands were cut into fine pieces under physiological salt solution. These pieces were placed in a mortar and ground into a homogeneous mass, 400 c.c. of sterile salt solution being added. This was then filtered through sterile gauze and given as a transfusion into the patient's breast at 10 P.M. At 1.30 A.M. on the following morning, she was asleep and the contractions were becoming less violent. They disappeared in her hands, arms, and face by 10 A.M. and her lower extremities were nearly relaxed. The temperature dropped from 38.5° C. at 8 P.M. on the second day after the beginning of the attack to 36° C. on the third day. There were no more contractions until the fifth day, when there was a recurrent attack lasting twenty minutes, and involving only the face. This was succeeded by milder attacks which lasted until about 11.30 P.M. at which time she was given two parathyroids subcutaneously in 100 c.c. of salt solution. The attack

ceased almost immediately, and the patient has remained free from any symptoms of tetany up to the present time, more than a year after the operation. The permanent results are probably due to the fact that parathyroids were not all removed. The parts left were undoubtedly so damaged by the traumatism of the operation that their functions were suspended; but as they recovered, their normal work was resumed and possibly compensatory hypertrophy was secured.

**Musculospiral (Radial) Paralysis Due to Dislocation of the Head of the Radius.**—STETTEN (*Annals of Surgery*, 1908, xlviii, 275) says that musculospiral paralysis as a result of dislocation of the head of the radius is a distinct type of nerve injury, and is quite as definite and characteristic as any other form of injury to this nerve. In fact, in every case of anterior dislocation of the head of the radius the two divisions of the musculospiral nerve are in danger and it is a fortunate accident if they escape. Its actual occurrence is naturally rare, but comparatively, that is, compared to the frequency of the joint injury itself, it is not infrequent. It is most likely to occur when the dislocation accompanies ulnar fracture and when the direction of the dislocation is forward and slightly outward. The nerve is almost invariably injured below its point of division into the posterior interosseous and radial. One or both branches may be caught by the dislocated head. The symptoms are practically those of the typical musculospiral palsy. They may vary greatly in extent or degree, depending upon whether one or both nerves be injured and how badly. The supinator longus muscle escapes involvement. The prognosis is good under appropriate treatment, which is practically the same as that for the dislocation: simple reduction, if possible, and generally resection of the head of the radius in old cases, with nerve suture if necessary. Should the nerve be uninjured in a dislocation of the radial head, its close proximity to the head of the bone should be borne in mind, the dislocation should be reduced, and care should be exercised not to injure the nerve by pressure, hyperextension, or careless operative technique.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**Clinical Observations on the Intravenous Use of Strophanthin.**—LUST and HOEPFFNER (*Deut. Arch. f. klin. Med.*, 1908, xcii, 282, 485) relate their experiences with the intravenous use of strophanthin. Lust gives detailed histories of some especially instructive cases; Hoepffner bases his conclusions on observations in 34 cases. Both consider the action of

strophanthin very similar to that of digitalis, but stronger and more prompt. Lust's conclusions are as follows: (1) Acute cases of cardiac insufficiency in which digitalis works too slowly can be favorably influenced in a few minutes by a single injection of strophanthin; occasionally a second dose may be necessary. (2) A diminution of the pulse-rate with an increase in the size of the individual beats occurs in a few minutes, increased diuresis follows after a few hours, and the general condition improves. (3) Given in combination with digitalis it serves to increase and maintain the digitalis stimulation; for this purpose it should be given in small and repeated injections. (4) It should be given in doses of 0.5 to 1 milligram; often 0.3 milligram will be sufficient to begin with. (5) To prevent a cumulative action, injections of 1 milligram should not be repeated oftener than once in twenty-four hours. (6) It is of no therapeutic value in nephritis when other diuretics fail; it may be of diagnostic value and point the way to subsequent therapy in those cases in which it is doubtful whether the insufficiency is cardiac or renal. (7) It is of no value in pneumonia.

In five cases of pneumonia, Hoepffner saw improvement of the circulation only once. From this he does not draw any conclusions; furthermore, he thinks strophanthin was probably given too late. He also suggests, as an additional reason for its failure, that in pneumonia the paralysis of the vasomotor system is the chief cause of the failure of the circulation. Hoepffner observed two cases of acute heart failure during convalescence after infectious diseases, in both of which the subjective and objective symptoms promptly disappeared after the injection of 0.5 milligram of strophanthin. In pulmonary tuberculosis no diminution of pulse-rate was obtained, although the size of the pulse seemed increased. Hoepffner sums up the indications for the use of strophanthin as follows: (1) Severe cardiac insufficiency, in which digitalis has lost its effect. (2) To re-inforce digitalis therapy and to shorten the period of use of digitalis. (3) Cases of cardiac insufficiency in which other means have failed.

With regard to bad results, chills at first were frequently observed, but since the perfection of the preparation for intravenous use they no longer occur. Lust had one case in which death occurred fourteen hours after an injection of 1 milligram. He thinks this death had no connection with its use. Hoepffner had two fatal cases. One died three minutes after the injection of 1 milligram, too short a time for any poisonous drug action. This case was a severe case of failure of compensation, and he thinks death was coincident with the injection, but not caused by it. The second case (one of the early ones), died during a chill. He thinks this death could now be avoided with the perfected preparation.

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**The Use of Fresh Animal Sera in Hemorrhagic Conditions.**—LEARY (*Boston Med. and Surg. Jour.*, 1908, iii, 73) says that the power of blood sera and tissue juices to promote coagulation has been known for some time to physiologists. The practical application of this knowledge is due largely to the work of Weil, who first used fresh animal sera in hemophilia. Weil's work brought out these facts: That the blood serum of horses, of rabbits, and of beef creatures, as well as human serum, would control hemorrhages by increasing the coagulability of the

blood; that beef serum was too toxic for ordinary use; that the serum should be less than two weeks old; that a dose of 15 c.c. intravenously or 30 c.c. subcutaneously would usually obtain results; that the local use of serum favored clotting, and that the increased coagulability persisted for fifteen days to several weeks. In hereditary hemophilia the results, at best, were temporary; repeated injections were necessary to control hemorrhages, and the greatest value of the treatment lay in the prophylactic injection of serum before operative procedures. In sporadic hemophilia and acute purpura the cures were usually permanent.

Diphtheria antitoxin has been used with variable results in the control of hemorrhages, probably because of the difficulty of obtaining a fresh antitoxin. It seems that commercial antisera are subject to the same objections. Leary advises rabbit serum, which should be less than two weeks old. He prefers to use it subcutaneously, since the dangers of hemolysis and thrombosis (although remote) are to be considered in the intravenous use. The latter, he believes, should be limited to extreme cases or to those in which human serum is used. The toxic action of horse or rabbit serum is slight, although beef, goat, and sheep sera are often notably toxic. Although rare in human beings, the danger of anaphylaxis, when it is necessary to repeat the injection, is to be considered. As a rule, however, only one injection is required. In one case, when the bleeding was repeated, guinea-pig serum was used for the second injection. Leary had no evidence of toxic action, other than one case of urticaria. From his observations he believes that the serum also acts as a cardiac stimulant. From a series of twenty cases he does not attempt to draw definite conclusions, but believes that the results of Weil, with his own cases, suggest a wider use of sera in the control of hemorrhage, especially its prophylactic use before operations.

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**Milk-free Diet in Typhoid Fever.**—SEIBERT and STRONG (*Medical Record*, 1908, xxv, 1017, 1018). Seibert has used milk-free fluid diet in 61 cases of typhoid fever, with only 1 death. His routine is as follows: An initial calomel purge, two grains repeated in two hours. For the first twenty-four hours cold water only is given by the mouth. Rectal irrigations of three pints of warm water are given every three hours in severe cases, in average cases every six, and in mild cases every twelve hours. Intestinal hemorrhage, appendicitis, and perforation are the only contraindications. One-half pint of strained rice, oatmeal, or barley soup, containing the extract of one-half pound of meat and egg yolk, is given every three hours. The patients are not urged to take the full amount, but only as much as is palatable. They are made to drink freely of cold water. At the fifth or sixth day the patients usually desire more food, and this is met by making the soups thicker. About this time strained pea, lentil, potato, and tomato soup with rice are added. At the end of a week, two or three pieces of zwieback are given if the patients are hungry. No egg albumin is allowed, because of the possibility of formation of toxins. Diluted hydrochloric acid is given before the feedings. No alcohol is necessary unless the patient is accustomed to its use. The results of this treatment, Seibert thinks, are that the mortality is reduced, the attack is shortened, most of the patients convalesce much sooner, complications are diminished, and both the intestinal and nervous symptoms are ameliorated. In his series of cases the nausea,

headache, delirium, insomnia, tympanites, and diarrhoea disappeared in two or three days and did not recur. In the majority of cases the temperature reached normal on the ninth to the twelfth day of the treatment. In a smaller number of cases this occurred within the first week. In cases admitted with complications, these disappeared more readily than under the former milk diet. Strong has treated seventeen cases, and thinks very favorably of this mode of treatment. He believes it eliminates fermentation, one of the principal sources of danger. He uses broths, crackers, zwieback, gelatin, rice, etc. His results were: There was less prostration, the tongue remained moist and clean, there was no tympanites or diarrhoea, and the patients maintained their weight better.

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**Antityphoid Inoculation.**—SANBORN (*Boston Med. and Surg. Jour.*, 1908, clviii, 864) states that statistics show that the incidence of typhoid fever among inoculated individuals is about one-half that among those not inoculated, and that among those who contracted the disease after inoculation is about one-half that in subjects who contract the infection and are uninoculated. As to the reasons for the incidence of the disease in those inoculated we may speculate that in some instances there was insufficient response to the vaccine given, in the formation of protective substances; in some it is possible that improper dosage may prevent the induction of protection; in some infection may have taken place during the period of diminished resistance that experiment has shown follows the injection of any bacterial vaccine of sufficient dosage to later cause an increase in antibacterial substances. At this period there must be greater susceptibility to infection. In other individuals inoculation may have been given after infection had taken place, but before the development of symptoms. The danger of the inoculation of a properly made vaccine, standardized and given in proper dosage, should be nothing and the subsequent symptoms are not to be dreaded. The protection achieved may continue for two years or more.

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**Antityphoid Inoculation in the British Army.**—LEISHMAN (*Military Surgeon*, 1908, xxii, 421) gives the results of antityphoid inoculation in the British Army in India as follows: Non-inoculated, 8113. Of these 173 individuals contracted the disease and 42 died. Incidence per 1000, 21.32; mortality per 1000, 5.18. Inoculated, 2207. Of these 15 contracted the infection and 3 died. Incidence per 1000, 9.80; mortality per 1000, 1.36. The duration of the immunity conferred cannot yet be said to be established. Much importance is attached to the possibility of the development of a negative phase of resistance to infection following inoculation, but it appears that the dangers of this phase are more theoretical than real. Now and then a subject will be inoculated who is in the incubation period of the disease, but, apart from this, there seems to be no evidence that recent inoculation increases the liability to infection.

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**Vaccines in Tuberculosis.**—WEBB (*Ill. Med. Jour.*, 1908, xiii, 607) has used, in this form of treatment, almost entirely Koch's new tuberculin. The initial dose has never been greater than  $1\frac{1}{100}$  mg., and

often as low as  $\frac{1}{100000}$  mg., a dose which has been shown capable of producing a positive phase. Upward of 60 patients, chiefly of pulmonary tuberculosis, have been inoculated with gradually increasing doses up to not exceeding  $\frac{1}{800}$  mg. at intervals of from seven to ten days. In all patients the opsonic index has been determined to eliminate any possibility of auto-inoculation, but the index has not been used as a guide to time for inoculation, but only as a test to ascertain if the desired effect has been brought about. The results have been most pleasing, showing a distinct gain over former results obtained by a combination of climatic and sanatorium treatment without tuberculin inoculations. The results from the use of Koch's new tuberculin have been most favorable, no bad effects having been noted in any subject. Several moderately advanced infections have been apparently cured. Many seem to have been arrested from an active condition which rest and climate alone could not achieve. Febrile patients have been rendered afebrile, and especially when tuberculin has been combined with mixed vaccine, marked alleviation of cough, and expectoration has been common.

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**The Treatment of Intermittent Lameness.**—KOLMER (*Univ. Penna. Med. Bull.*, 1908, xxi, 80) considers the treatment of this condition in most instances unsatisfactory. If there is a syphilitic element, a thorough course of mercury and the iodides may both arrest progress and relieve symptoms. Potassium iodide may be given in the belief that it is a vascular stimulant and promotes the flow of blood through the vessels, thus furnishing the muscles with the needed blood. If arterial tension is high the nitrites should be prescribed. Alcohol, tobacco, over-exertion, and exposure should be avoided, and massage and passive movements, mud, and other warm baths with galvanism to correct vasomotor irritation, together with the correction of flat foot, if it exists, offer some hope of success.

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**The X-rays in Lupus.**—TOMKINSON (*Practitioner*, 1908, lxxx, 817) quotes Gaucher as stating that phototherapy gives very good results in the two varieties of lupus. It has the merit of giving in general, beautiful cicatrices, but it is a long and costly process, not within the reach of everybody and is not applicable to every region. The Finsen method remains at present the best. Radiotherapy has an analogous action to, but more intense than, phototherapy upon tuberculous lupus. It is more difficult to control. Tomkinson is accustomed to employ for facial lesions a combined treatment, which so far has given good results. The technique is as follows: Crusts are removed by a salicylated ointment. A tentative x-ray exposure of from three to five minutes is made upon a small area of the lesion. In a few days the rays are directed for about five minutes daily upon a wider area until the whole lesion has been exposed some three or four times. It is then plastered with Unna's 50 per cent. salicylic acid and creosote plasters, which is renewed daily. If this is badly borne the lesion is previously swabbed with 10 to 20 per cent. cocaine. In about ten days much of the tuberculous tissue will have come away. The lesion is then swabbed with cocaine solution, dried and painted with phenol, 0 parts; lactic acid, 15 parts; salicylic acid, 15 parts; absolute alcohol,

20 parts. A few minutes later the lesion is painted with phenol, 80 parts; absolute alcohol, 20 parts. After cauterization a dressing of 1 to 30 carbolic oil is applied for a day or two, to be followed by 20 per cent. aqueous solution of ichthyol until healing has taken place. Subsequent similar courses of treatment are sometimes necessary.

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**Camphoric Acid.**—TYRODE (*Boston Med. and Surg. Jour.*, 1908, clviii, 908), after having performed over 100 experiments upon animals with this substance, concludes that camphoric acid as such acts in the same manner as other organic acids which are not decomposed in the body, that in combination as a sodium salt, which is formed in the intestines, it acts like any neutral salt, such as sodium sulphate, that is, its ions have so little activity that it possesses only the action derived from its physical properties, "salt action." He further sees no justification in its use as a respiratory and heart stimulant, nor as an anhydrotic in the night sweats of tuberculosis. Yet it may be of some utility as a urinary antiseptic, because it may have, in common with many other free organic acids, slight antiseptic power.

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**Results of Treatment of Epidemic Meningitis with Flexner's Serum.**—SLADEN (*Johns Hopkins Hospital Bull.*, 1908, cciv, 245) says that during the years 1889 to 1907 there were 33 cases of epidemic cerebrospinal meningitis treated at the Johns Hopkins Hospital, of these 21 died and 12 recovered, a mortality of 64 per cent. In 1908 there were 19 cases, all of which received the Flexner antimeningococcic serum. Of these, 16 recovered and 3 died, a mortality of 16 per cent. Of the cases that died, 1 was fulminant; 1, a child aged twenty-nine months, was admitted on the fourteenth day of the disease and died forty-eight hours after admission; the third was a stout colored woman with a complicating bronchopneumonia, who died forty-eight hours after the first dose. Most of the cases were temporarily upset by the injections, complaining of pain, usually in the knees, occasionally in the hips, and on two occasions pains about the rectum and a desire to defecate. The pains lasted from two to ten hours after the injection. Following the injections there was usually a slight rise in temperature and increased restlessness. Urticaria and erythematous eruptions were not infrequent. Usually there was an interval of from twelve hours to three days before any improvement of symptoms. Some of the cases required only one injection, others as many as six. The serum was given daily until the temperature became normal, and if there was any recrudescence of the fever, the serum was again used. By this treatment there was obtained a fall of temperature, often by crisis; an early subsidence of delirium; the headache, the pain in the neck and back, and the general hyperesthesia were much alleviated. Strabismus, stiffness of neck, and Kernig's sign were more persistent. An increase of the polymorphonuclear neutrophils was noted in the spinal fluid after the injections, and the meningococci seemed to become more intracellular.

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**Poisoning by Bismuth Subnitrate.**—MEYER (*Therap. Monatsh.*, 1908, viii, 388) cites three cases of death resulting from large doses of bismuth subnitrate. In 1906 Benneke and Hoffmann reported the death of an infant who had been given 3 to 4 grams of bismuth in 100 c.c. of butter-

milk; it was supposed that the poisoning was due to some chemical change caused by the lactic acid, though this did not explain the methemoglobinemia found at autopsy. Böhme (*Arch. f. path. Pharm.*, 1907, lvii, 441) reported the sudden death of an infant who had been given bismuth emulsion by mouth, and after an interval of two days, several grams by rectum. Three hours after the rectal dose she was seized with abdominal pains and diarrhoea, accompanied by steadily increasing cyanosis and marked dyspnoea. The heart was markedly overacting and the pulse was small and feeble. Death occurred in half an hour. At the autopsy traces of nitrous acid were found in the blood and pericardial fluid, though no metallic bismuth was found in the blood or liver, as had been the case in Benneke's patient. Böhme, by chemical means and by experiments on animals, established that nitrites can be formed from bismuth subnitrate in sufficient quantities to cause death. He found that human feces, and especially that of infants, was capable of reducing nitrates to nitrites. From this he thinks that it is possible for nitrites to be formed in poisonous amounts when large amounts of bismuth subnitrate are brought in contact with feces rich in bacteria, but, at the same time, that ordinary therapeutic doses do not have this effect. Meyer's own case was a man, aged twenty years. Three hours after a dose of 50 grams of bismuth subnitrate, given for radioscopic examination, he suddenly became markedly pale and cyanosed with all the symptoms of collapse. He was freely stimulated, but died in a few hours. In a note there is also an account of three other cases who recovered after alarming symptoms of similar nature. To prevent this Meyer advises that bismuth carbonate be used. Bismuth hydroxide has been suggested, but this does not remain in suspension long enough to permit the necessary examination.

## OBSTETRICS.

UNDER THE CHARGE OF

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**The Prognostic Value of Changes in the Blood in Puerperal Diseases.**—GRÄFENBERG (*Archiv f. Gyn.*, 1908, Band lviii, Heft 2) concludes a very interesting study of this subject. The absolute leukocyte count and the leukocyte curve do not give positive indications as to the severity of a puerperal complication. When the leukocyte curve is recorded for a long time it gives information of comparative value in connection with other symptoms. When the neutrophiles are greatly increased they indicate a condition seriously threatening the organism, and when polynucleosis in high degree is present, if for a long time, it indicates severe disease. When the neutrophiles are above 70 per cent. and the leukocytes above 10,000, it is safe to infer that suppuration has occurred. Exceptions, however, to this rule are observed and must



be kept in mind. The eosinophiles disappear from the consideration of the blood when a severe puerperal infection develops, and coma again under observation when the disease has reached its highest point. They are of no value as indicating the severity of a condition or its probable fatal termination. The eosinophile leukocytes are of value in puerperal gonorrhoea, in which their increase or their failure to disappear points out the nature of the infection. An increase in the large lymphocytes indicates an unfavorable prognosis, while an increase of the small elements points toward an improvement in the patient's condition. When there is a reversal of the usual relation between the two forms, the indication is unfavorable. In convalescent patients there is a characteristic lymphocytosis, sometimes reaching 73 per cent. of which 69 per cent. were small lymphocytes. When the increase is in the large lymphocytes only, the indication is unfavorable. The neutrophile appearance of the blood shows a lessening of the nuclei. This is most pronounced in fatal cases of purulent peritonitis. When the nuclei increase rapidly the prognosis is favorable. In severe puerperal gonorrhoea the nuclei curve is very little, if at all, less than normal. Attention is called to the importance of not laying too much stress on the nuclei curve alone in the matter of prognosis; other facts relating to the blood must be taken into consideration; especially important is the curve of the small lymphocytes.

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**Axillary Mammary Glands.**—KAYSER (*Archiv f. Gyn.*, 1908, Band lviii, Heft 2) reports 4 cases with illustrations of axillary mammary glands. As a rule the patients were but little inconvenienced by this anomaly when not in a pregnant condition. In some cases slight pain was occasionally experienced by movements of the arms during menstruation; and some patients complained of neuralgic pains. In one instance severe neuralgia of the brachial plexus during menstruation was cured by the removal of the axillary mammary glands. During the last months of pregnancy patients sometimes suffer from the swelling of these glands. During the puerperal period they often become exceedingly tense and give rise to considerable pain. The swelling is greatest from the sixth to the eighth day, disappearing from the tenth to the twelfth day. In one instance primary carcinoma developed in one of these glands.

So far as treatment is concerned they require no interference unless they become excessively painful, or show evidence of infection or malignant development. From the standpoint of embryology they result from the excessive development of gland tissue along the mammary ridge of the embryo.

## GYNECOLOGY.

UNDER THE CHARGE OF

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**Preservation of the Ovaries Entire or in Part in Supravaginal Amputation or Panhysterectomy.**—REUBEN PETERSON (*Amer. Jour. Obst.*, 1908, lvii, 633), after a careful study of 173 cases of his and a review of the literature, states that at least 10 per cent. of all women regularly menstruating at the time of operation will be free from the troublesome symptoms of the artificial menopause after hysterectomy with removal of the ovaries. The percentage of women with no symptoms after similar operations will be slightly more than doubled if some ovarian tissue be retained. The severity of the symptoms of the artificial menopause is much less when the ovaries are retained after hysterectomy. It is not necessarily true that the younger the woman the more will she suffer from the symptoms of the menopause, after hysterectomy with removal of the ovaries. The greatest percentage of suffering occurs in women operated upon between the ages of forty and forty-four years. Therefore, the rule that ovaries should be removed from patients over forty when hysterectomy is performed should not be followed. The frequency and severity of the artificial menopause is not influenced in any way by the kind of hysterectomy performed, whether the ovaries be removed or retained. The severity of the symptoms of the menopause is practically the same after hysterectomies with removal of the ovaries for fibroid disease of the uterus and inflammatory disease of the appendages. Retention of ovarian tissue after hysterectomy cuts short the period during which patients usually suffer from the symptoms of the artificial menopause. The greater the amount of ovarian tissue conserved, the more will the symptoms of the artificial menopause be mitigated.

**Transplantation of Ovaries.**—F. H. MARTIN (*Surg., Gyn., and Obst.*, 1908, vii, 7) reports 3 cases of heterotransplantation and 5 of homotransplantation, all of which he had done. After giving a thorough review of the literature of the subject he draws the following deductions: The operation of homo- or heteroplastic transplantation of the ovaries in women, or in lower animals, is no more dangerous if accomplished aseptically than any other small plastic operation on the appendages. Homotransplantation of ovaries in women, or in lower animals, will prevent the atrophy of the genitalia which usually follows castration. It is not yet satisfactorily demonstrated that heterotransplantation of the ovaries in a considerable number of cases will give permanent relief from the nervous symptoms produced by the menopause or prevent atrophy of the genitalia otherwise following castration. Heterotransplantation of ovaries in women, or in lower animals, may prevent the atrophy of the genitalia which usually follows castration. Transplantation of ovaries from one species into another may result in pre-

venting ordinary changes in the genitalia resulting from castration. Menstruation will continue in women and monkeys after homoplastic transplantation of ovaries. Conception has followed homotransplantation in animals, heterotransplantation in animals, homotransplantation in women, and has been reported following heterotransplantation of the ovaries in women. Heterotransplantation of the ovaries should be accomplished as soon after the primary operation, in which the receptor's ovaries have been sacrificed, as possible, before the menopause has become established and the genitalia atrophied. Transplanted ovaries in localities other than the normal will maintain their vitality, functionate, and prevent the ordinary sequels of castration.

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**Eversion of the Uterus.**—PIERRE DELBET (*An. de gyn. et d'obst.*, 1908, v, 329) describes the case of a multipara, aged forty-two years, who had been in his care during this attack of illness; he had frequently examined her believing the condition was that of a sloughing fibroid. At the operation he found the mass to be the inverted uterus. Delbet maintains that as the infolding began at the cervix and proceeded from there instead of from the fundus it should be called eversion and not inversion of the uterus.

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**Fallacies of Intra-abdominal and Atmospheric Pressure as Supports of the Uterus and Abdominal Organs.**—CHANNING W. BARRETT (*Surg., Gyn., and Obst.*, 1908, vi, 369) carefully considers this subject and by experimentation attempts to disprove the opinions held by various authors on it. Barrett's conclusions are: When lax ligaments allow abdominal organs to make undue strain upon the pelvic floor, bulging the lower part of the abdomen, the air would be pressing inward at the epigastrium and diaphragm. The abdominal organs are not held together, surface to surface, so that it is difficult for one to leave another. One moves as easily away from the other, and something else moves in to take its place, as though they were in a sac of mosquito netting. The uterus is an abdominopelvic organ and not a part of the pelvic floor. It lies normally above the pelvic floor and not against it, but is attached to it by means of the vagina. If the vagina is to be considered a ligament, it must be for support of the pelvic floor or to prevent ascent of the uterus. The uterus may come to lie upon the pelvic floor, but so may the other abdominal organs. The pelvic floor is, then, only indirectly a support to the uterus, as it is to other abdominal organs. With a weak pelvic floor we may have hernia of abdominal organs; first the bladder and rectum, then the uterus, and then other organs. The uterus is primarily supported by its ligaments, but may be partially carried by fluid pressure, or may be pushed downward by solid structures. With a weak pelvic floor the bladder, rectum, uterus, and ligaments may be called upon to do this work of the pelvic floor, and may succeed for a time, but are apt to rebel sooner or later and prolapse, especially with excessive intra-abdominal pressure. The pelvic floor is a very important structure in abdominal support. Injuries to this structure are often responsible for displacements of the uterus. When displacements have occurred, however, orthopedic work upon the ligaments is usually as necessary as repair of the pelvic floor for permanent relief; neither alone

is sufficient. The uterine ligaments, being the normal support of the uterus, should receive our attention when surgical work is necessary, rather than the creation of false ligaments. In increased intra-abdominal pressure, much may be accomplished by remembering that the contents of the abdomen are too great. Diet, exercise, massage, and appropriate positions, will accomplish much.

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**Primary Carcinoma of the Female Urethra.**—L. S. McMURTRY (*Annals Surg.*, 1908, xlvii, 1032) reports 2 cases and has collected 25 others in the literature. McMurtry states that early diagnosis of primary cancer of the female urethra is extremely difficult owing to its close resemblance to caruncle and syphilitic lesions. The treatment in early cases is surgical ablation. In 1 of his 2 cases the operation has been done over one year and no recurrence is evident.

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**Adeno-fibro-myxo-chondro-sarcoma of the Cervix Uteri.**—PUECH and MASSABUAU (*Ann. de gyn. et d'obst.*, 1908, v, 306) report a tumor of this kind removed from a nullipara, aged fifty-nine years. The menopause occurred at forty-six years, and four years later at stool she passed from the vagina a piece of tissue and considerable blood. Three years later Puech removed the grape-like tumor by severing the pedicle and applying the thermocautery. This tumor proved to be sarcomatous. Five years later, symptoms returning, an examination revealed another tumor; this was removed by hysterectomy and proved upon microscopic examination to be an adeno-fibro-myxo-chondro-sarcoma.

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**Ectopic Pregnancy in the Stump of an Excised Tube, causing Attacks of Intestinal Hemorrhage.**—H. M. VINEBERG (*Amer. Jour. Obst.*, 1908, lvii, 527) reports the case of a woman, aged thirty-three years, who had been married fifteen years and had had three children and several induced early abortions, and in September, 1908, the left adnexa removed for ovarian abscess. Pain in the region of the stump of the appendage persisted. During the two months preceding the first visit to Vineberg, November 13, 1907, she had had seven attacks of severe hemorrhage from the rectum, attributed to hemorrhoids, and menstruation was absent for a corresponding time. An examination revealed a mass attached to the left uterine cornu and which was diagnosed as a foreign body left at the operation. Three days later an operation revealed an unruptured pregnancy in the stump of the left tube, a part of the sac intimately adherent over a large area to the sigmoid. No opening between the two structures could be found. The sac was incised and contained a small amount of blood and an amniotic sac containing a foetus of eight weeks' development. The right adnexa were buried in adhesions and the right ovary contained a good sized corpus luteum. Vineberg found in a literary research but one case (J. C. Morfit, *Med. News*, 1900, lxxvi, 869) resembling this one; he mentions Keller's case (*Des grossesses extra-uterine*, Paris, 1872) of tubal pregnancy with fatal termination occurring subsequent to a supravaginal amputation of the uterus by Koeberle (Winckel, *Handbuch der Gebäur.*, vol. ii, 859); Wendeler's (*Beit. z. Geb. u. Gyn.*, Festschrift, A. Martin, 1895) of tubal pregnancy six years after vaginal hysterectomy, which at the end of the first eight weeks had vaginal hemorrhage; and Vautrin's case of tubal

pregnancy nine years after vaginal hysterectomy by morcellation for a large uterine fibroid (*Rev. med. de l'est*, 1908, xxxviii). Vineberg concludes that the hemorrhage in his case was due to the sigmoid being acted upon by the trophoblast, and comments on the failure of decidual reaction of the uterine mucosa and the external migration of the ovum.

**Successful Treatment of Chronic Gonorrhoeal Endometritis.**—G. KOLISCHER (*Surg., Gyn., and Obst.*, 1908, vi, 527) states that in this two special points are presented, viz., eradication of the gonorrhoeal infection and stopping the abnormal discharge. The method advocated was employed in the treatment of 43 cases, in 29 of which the treatment was persisted in until these two results were produced. Kolischer states that a drug, in order to be employed successfully on the endometrium, should be a strong germicide and should produce sufficient reaction to produce an intense shedding of the mucosa, but not sufficient cauterization for the production of an eschar, and that applications must be applied daily over an extended period of time. The routine employed is as follows: Test the uterus as to its reaction toward the introduction of foreign bodies into its cavity, by introducing carefully a sound to the fundus, under proper precautions, and accustom it to such invasion. Swab out the uterine cavity gently with a saturated solution of bicarbonate of sodium. Sometimes a tenaculum or a volsellum is fastened into the anterior lip of the cervix. A swab soaked in a 3 per cent. albargin solution is now introduced into the uterine cavity and allowed to remain five minutes; after its withdrawal a tampon carrying an ichthyol-glycerin solution of equal parts is placed against the portio, to be removed by the patient the next morning and be followed by a hot salt-water douche. A slight bloody discharge, following a few treatments, is a good sign and does not prevent continuation of the treatment. The applications are continued until the discharge ceases and the absence of pus and gonococci is demonstrated. The specimens should be taken after provocative influences have been active, such as during and after menstruation, twenty-four hours after the patient has taken some charged alcoholic beverages, or twenty-four hours after the mucosa has been touched with a 1 to 1000 bichloride solution. Occasionally the reaction from the albargin is obtainable only after the use of a sharp curette or swabbing with a 40 per cent. solution of formalin.

**The Pathology and Operative Treatment of Displacements of the Pelvic Viscera.**—W. E. FOTHERGILL (*Jour. Obst. and Gyn., Brit. Emp.*, 1908, xiii, 410) has written at length and dogmatically upon this subject, his recommendations being based upon his conception of the supports of the pelvic viscera as portrayed in his paper in the same journal last January. Fothergill regards classical prolapse of the pelvic viscera (descent of the uterus, appendages with the bladder, urethra, and vagina) as being due to elongation of the perivascular connective tissue in the base of the broad ligaments and extending laterally up to the internal iliac arteries, that such relaxation can never be removed and that, therefore, the surgical treatment is necessarily limited to plastic surgery of the vagina, perineum, and cervix plus ventrofixation. Fothergill believes a part only of this relaxation may occur, resulting in descent of the bladder and anterior vaginal wall, and even the posterior

wall. In such conditions only the lower portion of the supporting mass is affected, the upper part preserving its function; the treatment should be plastic. Again, Fothergill regards retroversion or retroflexion as due to the same character of relaxation occurring in the upper part of the pelvic viscera and recommends, when surgical treatment is needed, Alexander's operation when the uterus is movable and, if there are adhesions or diseased appendages, laparotomy with appropriate treatment of such complications and Webster's round-ligament operation. Apparently no instances of striking elongation of the uterus with recurrence of prolapse have been noted by him.

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**Treatment of Gonorrhoea in the Female.**—H. WELLAND HOWARD (*Jour. Amer. Med. Assoc.*, 1908, 1, 2136) relates a case treated by him in which, after application of 1 per cent. solution of nitrate of silver to the external urinary meatus, the cervix uteri and vaginal walls on alternate days, and later inoculating the vagina with the Doederlien bacillus, the gonococcus was found absent. At the beginning of Howard's treatment the tubes and ovaries seemed to be uninvolved; the cervix was red and not eroded, and near it was a dram of pus containing large numbers of gonococci or pus even when pressure was applied along the urethra.

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**Primary Cancer of the Fallopian Tube.**—LABUSQUIÈRE (*An. de gyn. et d'obst.*, 1908, v, 361) carefully considers primary cancer of the Fallopian tube and states that its diagnosis from pyosalpinx is practically impossible. Labusquière states it is the most malignant and most infrequent form of cancer of the female genitals, and that extension is along the sacral and the inguinal glands; that the Sanger-Barthe theory that it always has an inflammatory basis is untenable; that such phlegmasic changes as salpingitis, occlusion of the abdominal ostium, peritonitic adhesions and tuboövarian cysts can precede, but can also result from, cancer of the tube, and that the histological classification of papillary and papillo-alveolar cancer must be modified in the sense that papillary cancer represents the initial stage and the alveolar the ulterior stage of the papillary form.

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**Arteriosclerosis of the Uterus.**—R. B. SLOCUM (*Surg., Gyn., and Obst.*, 1908, vi, 352) reports a case of this condition and reviews the literature of the subject. Following Solowij, Slocum divides the cases clinically into two classes. In the first the hemorrhages are into the uterus, forming infarcts and usually accompanying a like condition in other vessels, the splenic artery being a common one; in the second class the hemorrhage occurs from the endometrium. The latter class is more readily recognized and treated. The first class is of interest principally to the pathologist. The second class occurs usually after the menopause, and the safest treatment seems to be hysterectomy.

## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

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UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,  
OF PHILADELPHIA.

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**Angioma of the Face, Mouth, Tonsil, and Rhino-epiglottic Fold.**—NAVRATIL (*Arch. inter. de laryng., d'otol., et de rhin.*, March-April, 1908) reports a case. An operation was attempted, but on anesthetizing the patient there was such an afflux of blood to the angioma during the period of excitation that symptoms of dyspnoea appeared, rendering immediate tracheotomy necessary. It was hence inferred that preliminary tracheotomy should always be performed in similar cases.

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**The Curing of Catarrhal Deafness by Cleaning Out the Fossæ of Rosenmueller.**—JERVEY (*Jour. Amer. Med. Assoc.*, May, 16, 1908) contends that many cases of catarrhal deafness and tinnitus aurium are due to impaired motility of the pharyngeal extremity of the Eustachian tubes, the result of granulation tissue or of hypertrophied lymphoid tissue in the fossæ of Rosenmüller, or to restriction by bands of tissue in sequence of the previous inflammatory conditions. These being scooped away with the forefinger passed behind the palate, hearing improves at once or within a few hours. To prevent recurrence the raw surfaces are mopped with a solution of silver nitrate or of argyrol every forty-eight hours for from ten days to two weeks.

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**Rhinœdema with Polyp Formation.**—HITSCHLER (*Penna. Med. Jour.*, August, 1908) reports a case of his own and three other cases. No organic disease was present in any of these five cases. Their most marked features, as of others not referred to, were the absence of inflammatory reaction and the recurrent nasal œdema, whether simple œdema or as a polyp.

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**Orbital Abscess Secondary to Nasal Disease.**—REBER (*Penna. Med. Jour.*, August, 1908) reports two cases, one the result of acute purulent sinusitis and the other a sequence to purulent rhinitis which had been set up by the presence of a foreign body—a swollen white bean—occluding the left nasal fossa.

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**Four Frontal Sinuses.**—MARTIN COHEN (*Jour. Amer. Med. Assoc.*, June 6, 1908) reports a skull which otherwise presented no unusual anatomical features, in which there were present on each side of the frontal septum two sinuses, one posterior to the other, and each having a distinct and separate nasal frontal duct which drained into the middle meatus of the nose. A complete bony septum separated the sinuses on each side.

**Operations on the Frontal Sinus.**—BECK (*Jour. Amer. Med. Assoc.*, August 8, 1908) describes in detail and illustrates a new method of exposing and operating upon the frontal sinus without deformity. The main feature consists in raising an osteoplastic flap, after bearing the skull by means of an incision through the skin and connective tissue along the upper margins of the eyebrows, then downward a short way upon the nose, and then across the bridge. This skin and subcutaneous flap is then dissected upward as far as required and as had been determined by radiogram beforehand. After the operation the osteoplastic flap is replaced and the skin flap brought down and sutured with silk-worm gut.

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**Sarcoma of the Septum and Rhinopharynx.**—WILLIAMS (*Jour. Laryn.*, July, 1908) reports the case of an unmarried woman, aged twenty-five years, who had been admitted to the Bristol Royal Infirmary for nasal obstruction and severe and recurring epistaxis after the attempted removal of a supposed nasal polyp. Access to the growth was made by raising an osteoplastic flap, and then nearly the whole septum was removed up to the anterior margin of the cartilage, the left ethmoidal cells and middle turbinal were likewise cleared away back to the sphenoid sinus, and the growth itself was also cleared away from the roof of the rhinopharynx. The osteoplastic flap was finally pushed back into position and sutured. Recovery was uninterrupted without any facial defect or deformity whatever. There had been no recurrence at the end of six months.

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**Streptococcic Infections of the Pharyngeal Adenoid Tissue in Adults.**—From ten cases occurring in her own private practice, DR. ALICE G. BRYANT (*Jour. Amer. Med. Assoc.*, June 13, 1908) calls attention to streptococcic infections of the pharyngeal adenoid tissue in cases with symptoms similar to those occurring in pulmonary tuberculosis, malaria, typhoid fever, or influenza. In the discussion of this paper Dr. Shurly stated that the serious sequels and complications of the infectious diseases, such as influenza, typhoid fever, diphtheria, scarlet fever, measles, tonsillitis, arthritis, and others, are in direct proportion to the absorption of toxin from the rhinopharynx—a pathological and therapeutic principle not sufficiently recognized by the average general practitioner.

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**Œsophagoscopy in a Sword Swallower.**—HALD (*Arch. inter. de laryng., d'otol., et de rhin.*, March-April, 1908) reports his observations in œsophagoscopy upon a sword swallower. The œsophagus had been very largely distended in consequence of the professional feats, and the cricoidean zone of the pharynx was patent and much larger than normal. There was an excoriation upon the posterior wall of the cricoid cartilage. Curiously, the patient could not support the examination any better than ordinary subjects, his œsophagus seeming to have become habituated to flat foreign bodies, but not to cylindrical ones. The mucous membrane was of a deep violaceous red, the result of chronic inflammatory condition, likewise the result of his sword swallowing. The tube could be introduced 45 cm. without reaching the cardia.



**Foreign Body in the Left Bronchus Discharged in a Mass of Pus on Bronchoscopic Examination.**—C. COMPAIRE (Arch. inter. de laryng., d'otol., et de rhin., May-June, 1908) reports a case of foreign body—a scale of a pine cone—in the left bronchus of a child, aged seven years, which had been in position for more than twelve months, and had produced an extensive purulent bronchopulmonary abscess. The extent of the abscess was revealed by radioscopy, but the foreign body was located. Bronchoscopic examination under chloroform lead to a continuous drainage of the abscess, in the last mass of which the pine scale was embedded and expelled on withdrawal of the instrument, after which the patient made a rapid recovery.

**Thymectomy and Thyroidectomy in a Child, Aged Twenty-three Days.**—SCHWINN (Jour. Amer. Med. Assoc., June 20, 1908) reports a case of enlarged thymus gland revealed by radiography, which was associated with an enlargement of the left lobe of the thyroid gland. The thymus gland was removed after splitting the sternum, a small piece of the left lobe being left in position for physiological purposes. The enlarged lobe of the thyroid gland was then resected in such a way as to save the parathyroid glands and recurrent laryngeal nerve. The patient made an excellent recovery and had gained three pounds in weight at the time of the report.

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## PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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**Protective Inoculation against Plague.**—R. P. STRONG (Jour. Med. Research, 1908, xviii, 325) reports at length upon the various methods of immunization which have been proposed against plague and upon the relative merits of these different measures: the inoculation of killed cultures, of living attenuated cultures, of filtered cultures, and extracts of artificial and of natural plague aggressives, and of inoculation according to Klein's method. The comparison of different methods seems to indicate that, while it is obvious, for several reasons, that for immunization in man in general the inoculation of killed cultures or extracts is far preferable and safer than the method of bacterial vaccination, nevertheless it would appear that in plague only by vaccination, with attenuated culture, can a satisfactory immunity be obtained. The usual adult dose is one twenty-four-hour agar slant culture, and children one-half to one-third of this amount of a strained culture designated "pest avirulent." Even in using these large amounts no severe reactions have been found. Usually, in a few hours after the vaccination, the temperature rises a little and declines on the following days to normal.

Sometimes there is a moderate leukocytosis. The deep, intramuscular injections are followed by induration which gradually subsides in a couple of days; no visible suppuration has ever occurred. The tissues when examined in animals showed that the organisms were still numerous after from six to eight hours, but in twenty-four hours none could be cultivated from the tissues. The process of immunization, then, was similar to that in a true vaccination, the organism reproducing itself in the tissues for some generations, then successive groups of receptors stimulating the production of corresponding groups of amboceptors in the animal body. In the vaccination of a large number of human beings, owing to individual variations in susceptibility to plague infection, all will certainly not be protected against the lethal infection by a single vaccination, but certainly a good proportion will be partially immunized and the immunity may last for some months. Therefore, it may frequently be necessary, as in smallpox vaccinations, to repeat and even use larger doses if necessary. It appears that the attenuated cultures, when carefully watched and tested, are of little danger in the vaccination of human beings. Nevertheless the work must be carefully carried out in many different races and classes of people before it can be adopted for general use. However, as the other measures have proved somewhat inadequate in the suppression of plague, this method of vaccination holds out, in certain endemic centres, greater hope of success in the suppression of this dread disease.

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**Polycythemia.**—LOMMEL (*Deut. Arch. f. klin. Med.*, 1907, xcii, 83) describes a case of polycythemia with moderate enlargement of the spleen. The red blood corpuscles varied between 9,700,000 and 10,200,000. The hemoglobin was 140 per cent., the white blood cells 5300. In smears of the blood, scattered nucleated red blood cells were seen. The viscosity of the blood was much increased and was estimated at 11.2 against a normal of 5. The absorption capacity of the red blood cells for oxygen was tested at room temperature and the co-efficient of absorption was found to be 1.01. Finally the respiratory exchange of gases was investigated by the method of Zuntz-Gleepert. The mean of the total respiratory volume for three days was 8561 cm. per minute, which is more than that given by Magnus Levy for the upper limit of normal (4500 to 7000 cm.) The average output of CO<sub>2</sub> pro kilo per minute was 3.23, and the intake of oxygen 4.42. These figures, again, stand at the very upper limit of normal. Lommel also made estimations of the total amount of urobilin which was excreted in the urine and feces, to see whether, with the polycythemia, there was a decreased destruction of red blood corpuscles. In this case the total amount of urobilin eliminated in one day was 325 mg., a very large quantity. Since it was impossible to establish any cause for the polycythemia, such as disease of the heart or lungs, Lommel thinks that the condition was dependent upon a decrease in the capacity of the red cells for the absorption of oxygen.

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**Immunity in Rocky Mountain Spotted Fever.**—A few years ago it was shown by Ricketts that the spotted fever, so common in the Bitter Root Valley of Montana, could be transmitted to guinea-pigs

and monkeys by intraperitoneal inoculation of citrated blood from subjects ill with the disease. During the experiments it was noted that one attack of spotted fever renders monkeys immune to a second inoculation. RICKETTS and GOMEZ (*Jour. Infec. Dis.*, 1908, v, 221) now find that there is no authoritative example of two attacks of the disease in the same person in the region of the Bitter Root Valley, and their inoculation experiments on guinea-pigs and monkeys go to show that one attack of the disease confers a strong, active immunity. This immunity in animals is characterized by the presence of immune bodies in the serum, which are sufficient to neutralize an active virus, when virus and immune serum are inoculated together; or which will establish a passive immunity in healthy guinea-pigs. The blood or blood serum of an immunized guinea-pig also has slight curative power, and when injected during the first few days of disease will modify the severity of the infection or when given two or three days after injection of virus, will protect the animal against the disease. By the method of mixed immunization, in which virus and immune serum are given together, guinea-pigs may be made to acquire an active immunity against subsequent inoculation. Since it has been shown that the horse is susceptible to the disease, Ricketts and Gomez hold out the hope that a serum may be obtained which may be used for protective inoculation in man. In order that this serum may be efficacious it would have to be injected within a day or two following the bite of the tick, which insect they have already found transmits the disease to man.

**The Excretion of Hexamethylenamin (Urotropin) in the Bile and Pancreatic Juice.**—It has been known for some time that certain substances, such as potassium iodide, pass more or less readily into the bile, and at least one substance, potassium iodide, has been shown definitely to be excreted by the pancreatic juice. CROWE (*Johns Hopkins Hosp. Bull.*, 1908, xix, 109) has experimented with the excretion of urotropin, a substance, which on account of its disinfecting properties, might be of great value in destroying certain bacteria infecting the gall-bladder, and finds that when urotropin is given by the mouth it passes very quickly into the bile. Hexamethylenamin or its decomposition product formalin, is excreted directly by the wall of the gall-bladder as well as by the liver cells, for after ligation of the cystic duct in dogs, the substances could be found in the bile of the isolated gall-bladder as well as in the bile coming from the common duct. Following administration by mouth, the drug was rapidly absorbed in the dog and could be demonstrated in the circulating blood when it remains for twenty-four hours. It was found further, that the drug was secreted in the pancreatic juice of dogs and after intravenous administration of 1 gram appeared in the saliva and milk. The practical value of the experiments was borne out by the study of the affect of administration by mouth of urotropin upon infections of the gall-bladder in man. Urotropin was given to three patients with biliary fistula. In one of these the infecting organism was the colon bacillus. In the first case five doses of 15 grams each, or a total of 75 grains of urotropin, caused the bile to become sterile in twenty-four hours; in the second case after the administration of the same dose, the numbers of colon bacilli in bile coming from the fistula were greatly reduced; while in the third case the bile was rendered

sterile after nine days' treatment. In 2 other cases it could be demonstrated that hexamethylamin is excreted in the spinal fluid and synovial fluid.

**Experimental Leukemia in Fowl.**—Although leukemia has been described as occurring, not frequently in horses, swine, and dogs, it is comparatively rare in fowl. Attempts have been made by several observers to transmit the disease by various means from one animal to another, but so far all attempts have failed. In this country the disease has been described quite accurately in fowl by WARTHIN (*Jour. Infect. Dis.*, 1907, ix, 360) who, however, made no inoculation experiments. ELLERMANN and BANG (*Zent. f. Bakt.*, 1908, xlii, 595) found among a number of chickens one which showed distinct evidence of leukemia. There was marked anemia with a leukocytosis of 600,000. Of these cells 84 per cent. were large mononuclear lymphocytes. In the normal chicken the average number of leukocytes is about 30,000 and the percentage of large mononuclear cells about 40. The leukemic chicken was killed and an examination of the organs showed a marked similarity to the changes in leukemia as they occur in man. The liver and spleen were swollen and in the capillaries of the liver and the bone-marrow there were characteristic and extensive infiltrations of the large mononuclear cells. Portions of the liver, spleen, and bone-marrow were emulsified in salt solutions and injected intravenously into five healthy chickens. Two of the fowls developed, after two and one-half months, a blood picture resembling that in the case of spontaneous leukemia, and at autopsy the organs showed the same characteristic leukemic infiltrations. A second series of inoculations was made from the organs of one of these chickens into six healthy fowls, all of which developed exactly the same disease. The characteristic changes which typified the disease in all the fowl was the progressive anemia, the marked leukocytosis with relative increase in the large mononuclear cells, and the intravascular leukocytic proliferations in the bone-marrow and liver. The cause of the disease could not be discovered; cultures upon various media, and search for spirochetes and protozoa were made without success. Further experiments seemed to show, however, that the actual presence of the cells was not necessary in order to transmit the disease, for two out of five chickens, inoculated with a clear filtrate of the emulsion of organs, free from cells, developed typical leukemia.

**The Adrenals in Arteriosclerosis.**—The atheroma which has been observed so uniformly in rabbits, after intravenous injections of adrenalin, has suggested more than once that certain types of arteriosclerosis in man may depend upon some pathological changes in the adrenal glands. Indeed, Josué has described what he terms "hyperepinephrie" a functional hypertrophy, in the adrenals of 3 cases of arteriosclerosis in man. HORNOWSKI and NOWICKI (Virchow's *Archiv*, 1908, xcii, 338) have, in this connection, studied quite carefully the adrenals from 36 cases of arteriosclerosis and as controls the adrenals from 122 cases which did not show arteriosclerosis. The average weight of the adrenals from the cases of arteriosclerosis did not differ materially from the glands of the control cases. Histological examination of the glands, from the cases of

arteriosclerosis, showed some atrophy of the cells of the cortex with thickening of the capsule and general increase in connective tissue. No changes were noted in the medullary portion of the organs. Hornowski and Nowicki lay little or no stress upon these changes, for they found much the same alteration in many of the adrenal glands from the control cases, and consider that the lesion is secondary to some pathological process in another part of the body. Neither could they determine that the adrenals of rabbits, which had developed atheroma following repeated injections of adrenalin, differed essentially from the glands of normal animals. It may, therefore, be concluded that the adrenals from cases of arteriosclerosis do not show any specific anatomical alterations, and, if the sclerosis is in any way dependent upon alterations in the adrenal gland, it may only be possible to discover these changes by chemical investigations.

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**The Effect of Pilocarpine on the Output of Lymphocytes through the Thoracic Duct.**—Rous (*Jour Exp. Med.*, 1908, x, 329) has been able to confirm some previous investigations concerning a lymphocytosis following intravenous injections of pilocarpine. In the dog he finds that shortly after an injection of pilocarpine the total lymphocytes in the blood are very definitely increased. Intravenous injections of pilocarpine nitrate cause a rapid and considerable increase in the output of lymphocytes from the thoracic duct, and he has determined that this increased supply of lymphocytes accounts for the elevation of the number of lymphocytes in the circulating blood. Among some of the factors which are accessory for producing this large cell output in the lymph are quickened flow and dyspnoeic breathing, but he believes that the actual cause is as yet undetermined. It is possible that it is largely dependent upon some mechanical factor, and the explanation which Harvey has suggested, that the increased flow of lymphocytes is due to pressure brought to bear on the lymph nodes and spleen by the contraction of muscle, may be the correct one. Rous, however, could not confirm Harvey's observation that atropine prevents the appearance of a lymphocytosis after pilocarpine injections. These experiments go to show that mechanical factors may be responsible for a rapidly appearing lymphocytosis. They are also important inasmuch as they demonstrate that the contribution of the cells through the thoracic duct may be important in the production of lymphocytosis, and that this lymphocytosis is not dependent upon a direct migration into the blood of cells from the spleen, bone-marrow, and lymph nodes.

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**The Hemolytic Action of Blood Serum in Malignant Disease.**—During the last year Kelling has described a reaction which takes place with the serum of patients suffering with malignant diseases. If small amounts of blood serum from such patients are added to a suspension of red blood cells in salt solution, hemolysis takes place. The red blood cells were derived from several varieties of animals. The blood serum of normal individuals did not bring about hemolysis. Kelling, answering a criticism made by v. Dungern, reported later the results of 600 examinations. Of these cases 265 were suffering from carcinoma and of this number 119 (43.4 per cent.) gave positive hemolytic reactions. Of the 320 cases which were not carcinomatous, a positive reaction was

obtained only in 11 or 3.4 per cent. Crile and Beebe, using human red blood corpuscles instead of red blood cells from animals, have obtained much the same results. Weil has studied the hemolytic action of the blood serum from eight dogs with transplantable lymphosarcoma. He found that the sera of the dogs that had tumors, showed, without exception, a marked hemolytic action toward the red cells of healthy animals of the same species, whereas the red cells from dogs that had tumors were much more resistant. Serum from normal dogs possessed almost no hemolytic action. FISCHER (*Wien. klin. Woch.*, 1908, xlv, 882) has studied the hemolytic action of the blood serum, after the method of Kelling, in 4 cases of malignant disease and in 7 cases suffering from various other conditions. The serum from one-half the cases of malignant disease, 3 of which were carcinoma, possessed in repeated experiments hemolytic power for the red blood cells of various species of animals, but the reaction did not prove to be specific, for it was obtained in 2 cases of pernicious anemia, 1 of tuberculosis, 1 of chronic heart disease, and 1 of diabetes mellitus.

**An Especial Affinity of the Bloodvessels of the Kidney for Adrenalin.**—JONESCU (*Wien. klin. Woch.*, 1908, xxi, 513) noted during an experiment upon a rabbit whose kidney was in an oncometer, that very minute doses of adrenalin produced great decrease in the size of the kidney. These experiments were repeated and it was found that doses of adrenalin, which were so small that they produced no more effect upon the general blood pressure than injections of 1 c.c. of salt solution, caused great contraction of the vessels of the kidney, which could be estimated by the shrinkage in the size of the organ. These experiments seemed to show that the bloodvessels of the kidney are peculiarly susceptible to the influence of adrenalin. Indirectly the experiments bear upon the question of the relation between nephritis and the secretion of the adrenal gland. It is possible that a slight hypersecretion of the adrenal may bring about contraction of the vessels of the kidney with deleterious consequences, but without giving rise to an elevation of the general blood pressure.

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All communications should be addressed to—

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THE  
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OF THE MEDICAL SCIENCES.

DECEMBER, 1908.

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ORIGINAL ARTICLES.

**TREATMENT OF TETANUS WITH SUBARACHNOID INJECTIONS  
OF MAGNESIUM SULPHATE.**

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IN December, 1905, Meltzer<sup>1</sup> published the results of a series of experiments he had made with the idea of proving magnesium to possess inhibiting power over the processes of the body. Briefly, the conclusions were to the effect that intravenous injections of small amounts inhibit respiration and cause paralysis of the entire body; that when applied directly to a nerve in a 25 per cent. solution it produces complete nerve block; that when injected subcutaneously it produces deep narcosis with complete muscular relaxation; and that a subarachnoid injection of a 25 per cent. solution produces immediate anesthesia and paralysis of the posterior extremities of monkeys. Acting upon the final conclusion, the practical value of subarachnoid injections of magnesium sulphate as a means of producing surgical anesthesia was soon put to test, and in May, 1906, Blake reported 12 cases which had been thus treated by Haubold, Meyer, and himself. In these cases they had followed Meltzer's suggestion and injected 1 c.c. of a 25 per cent. solution of magnesium sulphate to each twenty to twenty-five pounds of body weight; a dose found to be about one-third the lethal dose for monkeys. The result was found not altogether practical, as surgical anesthesia did not appear for three to four hours and it persisted longer than was

<sup>1</sup> Medical Record, 1905, lxviii, 965.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, 1906, ii, 541; Annals of Surgery, 1906, xlv, 367.  
VOL. 136, NO. 6.—DECEMBER, 1908.

necessary. Its use as an anesthesia in surgery was then apparently given up with a passing recommendation in its favor in the treatment of aneurysm by compression, and in the performance of prostaticectomy, and of amputation in diabetic subjects and in patients in shock. The paper concludes with a report of 2 cases of tetanus treated by the intraspinal injection of magnesium sulphate to control the convulsions: one successful and one unsuccessful case. Since then there have been reported 11 cases of tetanus treated by the injection of magnesium sulphate: 8 cases, 3 of which resulted in recovery, by subarachnoid injections; and 3 cases by subcutaneous infusions with magnesium sulphate, all of which were successful. Since the method seems to promise a great deal in the treatment of tetanus, the following case is reported:

*Resume of the Case: Boy, aged seven years. Diagnosis: tetanus. Incubation seven days. Admitted on the tenth day. Eleven lumbar punctures were made within thirteen days, approximately 2.5 c.c. of a 25 per cent. solution of magnesium sulphate being injected into the meninges at each puncture. Extensive paralysis followed each injection and involved usually all the muscles, except those of the head, neck, and diaphragm, and lasted approximately eighteen to twenty-nine hours. The injections were followed several times by respiratory collapse, lasting eleven to fourteen hours, and the pulse dropped, though not to a dangerous level. Antitoxin daily for fourteen days, in doses varying from 1500 to 7000 units; copious saline enemas and infusions; and sedatives for a short time, were also used in the treatment.*

E. K., a male, aged seven years (Surgical number 22,789), was admitted August 16, 1908; discharged September 19, 1908. Ten days before admission, while playing in the street, the patient was knocked down by a passing wagon and struck upon the cobble stones of the gutter, receiving a lacerated wound of the left hand. During the evening of the seventh day after the injury the patient had "locked jaws," bit his tongue, and had considerable difficulty in swallowing. On the following day the patient's jaws "locked" several times, and there was occasional twitching of the muscles of the hands and legs. Upon the ninth day while lying in bed the boy was noticed to have flexion of the fingers and wrists, general muscular twitching, and occasionally "stretched himself" (mild opisthotonos). Upon the morning of the tenth day he could open his teeth only approximately an inch, and he was brought to the clinic for treatment.

On admission the following note was made: Upon the dorsum of the left hand is a granulating wound, about 4 cm. in diameter, the base of which consists of greenish, necrotic tissue. The glands of the axilla are barely palpable. The child does not look ill, is interested in his surroundings, and quite rational. At irregular intervals, without apparent stimulus or when suddenly aroused, as by being touched or otherwise surprised, he has a general tonic

contraction of all the muscles of the body; during such an attack "risus sardonius" appears, the right hand and arm are thrown upward and backward, the abdominal muscles are rigidly fixed, and the legs are held perfectly stiff in hyperextension. During these opisthotonic seizures the left elbow, wrist, and fingers (the wounded extremity) show marked spasmodic exaggeration of the flexion which is constantly present. The incisor teeth can be separated about 2.5 cm. During the period of observation, which lasted twenty minutes, the child had twelve convulsions, during two of which there was involuntary evacuation of the bowels. Routine examination of the chest was negative. The temperature was 100°, the pulse 80, and the respirations 20.

A diagnosis of acute tetanus of rather severe grade was made, and it was decided to attempt treatment by means of subarachnoid injections of magnesium sulphate, following the suggestion of Meltzer.

The estimated body-weight was sixty pounds. This estimate is probably high since the boy weighed but forty-one pounds on September 15.

*Injection 1.* August 16, 7.30 P.M. Under very light ether anesthesia a lumbar puncture was made, and a few cubic centimeters of clear fluid was withdrawn, apparently under no great tension; 2.5 c.c. of a 25 per cent. solution of magnesium sulphate was then gently injected, no special precautions being observed as to the speed of injection. The infected area on the left hand was then rapidly excised, the wound carbolyzed, and a dry dressing applied. An injection of 1500 units of antitetanic serum was made in the left thigh.

Within thirty to forty-five minutes all reflexes in the legs were abolished; however, at the end of two and one-half hours there was a convulsion, marked by trismus, hyperextension of the head, and involuntary movement of the bowels. This type of convulsion then recurred every fifteen to twenty minutes, either spontaneously or was precipitated by the slightest stimulus, as attempting to drink a sip of water. The legs were paralyzed and the reflexes absent, but in some of the convulsions the arms were moved. The child could not open the jaws any farther than before the lumbar puncture and was quite unable to take water. The temperature was 103° at midnight.

August 17. Convulsions of the above type continued in decreasing rate and severity, and by 4 A.M. (twenty and one-half hours) there were no muscular contractions below the arms, and the patient began to take liquids freely. At 10 A.M. (twenty-six and one-half hours) knee-jerks were present and motion was returning in the legs. By 2 P.M. his condition was about as on admission; he was unable to take liquids without precipitating a convulsion. The temperature reached 105.4° seven hours after the first injection.

*Injection 2.* At 4.30 P.M. lumbar puncture was done under chloroform anesthesia, and 25 c.c. of cloudy fluid withdrawn; injection

of 2.5 c.c. of 25 per cent. solution of magnesium sulphate immediately followed. This injection was followed by a profound reaction. There was, as usual, loss of knee-jerks and paralysis of the legs and abdominal muscles, but the most striking effect was upon the respiration, the rate of which dropped within three and one-half hours to eight per minute, and within four and one-half hours to six per minute, becoming shallow and gasping and varying greatly in amplitude. The pulse remained full and regular and there was no cyanosis. The patient was in profound coma, and not until 11.30 P.M. (seven hours) did any convulsive muscular action appear; at this time the facial muscles began to twitch irregularly and there was slight trismus. Antitoxin, 1500 units, was given in the thigh.

August 18. At 1.15 A.M. (nine hours) respirations were 6 to the minute, and each ended in trismus which was becoming very severe. This condition persisted until 5 A.M. (twelve hours) when respirations began to increase in rate and amplitude and by 6.30 A.M. had returned practically to normal. From their first appearance the twitchings of the facial muscles increased slowly, until at 5 A.M. (twelve hours) the convulsive seizures were occurring about once per minute. The tongue was bleeding from the continued traumatism of trismus. By 9 A.M. (sixteen hours) the boy began to take fluids freely and continued to do so all day. Drinking or any disturbance caused facial spasm and trismus, but not until 3 P.M. (twenty-three hours) did the knee-jerks return. At 5 P.M. (twenty-five hours) there was opisthotonos, which appeared twelve times within the next sixteen hours. During this severe respiratory disturbance there was a very free secretion of mucus which seemed to embarrass respiration somewhat; atropine,  $\frac{1}{160}$  grain, was administered hypodermically. During the day 3000 units of antitoxin were administered.

August 19. The effect of the second injection was so alarming that some little hesitation was felt about proceeding; the boy had been in profound coma and for twelve hours had been watched constantly, since the need for artificial respiration seemed imminent. The result of this hesitation, however, is shown, for during the first part of the day, that is, from midnight until 9.30 A.M. he was in practically continuous opisthotonos, convulsions occurring every two to three minutes. He had taken practically no liquids since midnight previously.

*Injection 3.* Chloroform anesthesia. At 9.30 A.M., 2 c.c. of a 16.6 per cent. solution of magnesium sulphate, a considerably smaller dose than formerly, was given. The cerebrospinal fluid obtained seemed normal, and but 5 c.c. was removed. The head was elevated somewhat to prevent the injected fluid from reaching the respiratory centre. During the first four hours there was a gradual loss of knee reflexes; they returned slightly by 5 P.M. (seven and one-half hours), at which time facial spasm again appeared for the first

time since the last injection. Five hours after the injection the boy began to take liquids freely. This injection was likewise attended with bronchorrhœa. At 8 P.M. (ten and one-half hours) general convulsions involving the whole body again appeared. During the day the patient was given 3000 units of antitoxin.

August 20. The convulsions increased in rate and severity and by 5 A.M. (nineteen hours) typical opisthotonic seizures were occurring every ten to fifteen minutes. In spite of this fact the boy took liquids well.

*Injection 4.* 11 A.M. Under chloroform anesthesia, 3 c.c. of slightly cloudy fluid was removed, and 2.5 c.c. of 25 per cent. magnesium sulphate solution was injected. At this time there was continuous opisthotonos; within twenty minutes spasm of the abdominal and leg muscles began to disappear; within one and one-half hours the knee-jerks had disappeared; and within three and one-half hours the jaw was well relaxed, but there was facial spasm and trismus with each expiration. For thirteen hours the boy was unconscious, and during this period there was another respiratory collapse; within two and one-half hours the respiratory rate began to fall, and within three and one-half hours respirations were weak, shallow, and only five to the minute, at which rate they remained for three and one-half hours; they reached normal rate and amplitude within eleven hours of the time of injection. During this period there was again considerable secretion of mucus, for which atropine was again administered. During the day 4500 units of antitoxin were administered.

August 21. The boy regained consciousness about midnight (thirteen hours), but in spite of the muscular relaxation he seemed unable to take liquids well because of difficulty in swallowing. He was, however, quiet and seemed comfortable. By 9 A.M. (twenty-two hours) the knee-jerks had returned; opisthotonos soon appeared, and by 4 P.M. (twenty-nine hours) was more marked than ever before.

*Injection 5.* At 4 P.M. 19.5 c.c. of spinal fluid was obtained, and 2.5 c.c. of a 25 per cent. magnesium sulphate solution was injected. Within one hour the knee-jerks had disappeared and the abdominal muscles were soft. Within two hours respirations became diminished in rate and volume, and within four hours were weak, shallow, irregular in rate and amplitude, and about five to the minute; they remained of this character for about an hour, when improvement appeared, and within fourteen hours from the time of injection they were again normal.

The boy was taking little or nothing and he was accordingly fed by the stomach tube, which procedure disturbed him not at all. 3000 units of antitoxin were given during the day.

August 22. The boy was unconscious until 6 A.M. (fourteen hours), at which time he evidently appreciated his surroundings. He remained rather stupid, however, and had to be fed with the stomach

tube. There was a gradual return of muscular tonicity by 5 P.M. (twenty-five hours), however, and when the patient was turned upon his side for lumbar puncture he was in opisthotonos and perfectly rigid.

*Injection 6.* At 7.30 P.M. 3 c.c. of turbid fluid was withdrawn, and 2.5 c.c. of a 25 per cent. magnesium sulphate solution was injected. A moderate respiratory disturbance followed; the rate began to drop within two hours and within four and one-half hours had reached nine to the minute, at which level it remained for three hours; it reached normal rate and amplitude within twelve hours. There was again great secretion of mucus. The child was again in coma. During the day he was fed by the stomach tube, and 9000 units of antitoxin were given.

August 23. During the day the patient was quiet and had no convulsions. He, however, was evidently growing weaker and seemed more stupid; he was taking nothing by the mouth. There was still profuse secretion of mucus. At 5 P.M. (twenty-one and one-half hours) the abdominal muscles began to stiffen; the legs were flaccid, and the knee-jerks were absent. The reflexes of the forearm were present. Trismus became marked. During the day 3000 units of antitoxin were administered.

August 24. A convulsion occurred at 4 A.M. (thirty-two hours since the last injection); by 8 A.M. (thirty-six hours) tonic spasm of the body was almost continuous, and opisthotonos was extreme, the body resting on the head and heels.

*Injection 7.* 9.30 A.M. Lumbar puncture; no anesthesia; 2.25 c.c. of 25 per cent. solution of magnesium sulphate was injected. This injection was followed by little respiratory disturbance. The usual paralysis followed; the patient was apparently weaker and becoming exhausted, and accurate observations upon the effect of the magnesium were impossible. He, however, remained quiet, and except for an occasional groan was apparently in comfort. During the day 7500 units of antitoxin were given. The patient was still fed with the stomach tube.

August 25. A mild convulsion was observed at 3 A.M. (eighteen hours); there was a steady increase in the muscular spasm, and by 6 A.M. (twenty-one hours) the patient was rigid and in extreme opisthotonos, which condition persisted until noon.

*Injection 8.* 12 M. Lumbar puncture; no anesthesia; 2.75 c.c. of 25 per cent. solution of magnesium sulphate was injected. This was followed by the usual paralysis which persisted longer than usual, and was attended by but slight respiratory disturbance. The mucous secretion was more marked than usual, appearing within three hours. Muscular relaxation was present throughout, except in the neck, which remained stiff. The patient was quiet and apparently comfortable, although one could not be quite certain that he was clear mentally. During the day he was fed by the



stomach tube and 1500 c.c. of antitoxin were injected into the thigh.

August 26. The boy remained very quiet. By 1 P.M. (twenty-five hours) the legs became more rigid; at 2 P.M. (twenty-six hours) general, mild convulsions appeared and increased rapidly in severity until at 8 P.M. (thirty-two hours) they were occurring almost every minute, being provoked by the mildest stimulation and throwing the boy into extreme opisthotonos.

*Injection 9.* 10.30 P.M. Lumbar puncture; no anesthesia; 3 c.c. of 25 per cent. solution of magnesium sulphate was injected. During the day 1500 c.c. of antitoxin were injected into the thigh and the patient was still fed with the stomach tube.

August 27. Following the lumbar puncture the boy rested quietly. At 5 A.M. (six hours) he was moving his hands and opened his eyes when spoken to, but did not reply. During the day he seemed much brighter and, except for occasional facial spasms, was quite free; during the afternoon he took liquids freely. During the day 3000 units of antitoxin were given. The patient was fed by means of the stomach tube.

August 28. At midnight (twenty-five and one-half hours) a moderately severe general convulsion appeared; general convulsions then increased rapidly in severity and frequency until by 4 A.M. (thirty hours) they were extreme, throwing the boy into exaggerated opisthotonos.

*Injection 10.* 5 A.M. Lumbar puncture; no anesthesia; 3 c.c. of 25 per cent. solution of magnesium sulphate was injected. This injection was followed by profound collapse; within five hours the temperature dropped to 95.2°, the pulse to 104, the respirations to 16, and the patient was comatose. The dose of magnesium was somewhat larger than usual, because of the severity of symptoms; this may account for the collapse, but it is to be noted that the patient was very weak, had been on artificial feeding for six days, and during the preceding twenty-four hours had had a diarrhoea. Under appropriate treatment the boy soon improved and by evening was in good condition and comfortable. He was given 3000 units of antitoxin during the day and was fed by stomach tube.

August 29. At 3 A.M. (twenty-two hours) there was a mild general convulsion, but the night was a quiet one and he was greatly improved. In the morning he responded to questions by nodding and could move his hands and feet. By 10 A.M. (twenty-nine hours) reflexes were beginning to return, but all muscles seemed rather relaxed except those of the neck, which was hyperextended. His mental condition improved during the day, but muscular rigidity slowly appeared and by 10 P.M. (forty-one hours) was rather severe, trismus being frequent.

*Injection 11.* 10 P.M. Lumbar puncture; no anesthesia; 2.25 c.c. of 25 per cent. solution of magnesium sulphate was injected. This

was followed by the usual paralysis. During the day 3000 units of antitoxin were injected. The patient was fed by the stomach tube.

August 30. The boy had a good night and during the afternoon began to take liquids freely. At 8 P.M. the following note was made: "Answers questions intelligently with yes or no. Opens teeth 4 cm. Good motion of legs and arms. Abdomen soft. Taking nourishment well. Voiding urine. No muscular rigidity. Knee jerks not exaggerated. Change in general condition within twenty-four hours is remarkable."

August 31. During the night there were several mild convulsions, but his condition in the morning was good.

During the next three days the boy was troubled with severe muscular spasm of the left hand and forearm; either spontaneously or upon slight stimulation the left forearm, wrist, and hand would go into violent flexion, which he was powerless to prevent and which caused him great pain. This condition gradually disappeared and his convalescence was without event except for an otitis media, which cleared up promptly, and several small abscesses, one of which came upon the occiput and was apparently due to the trauma sustained during opisthotonos.

September 19. The patient was discharged.

September 28. Examination is negative. There is no increase of reflexes, and no muscular rigidity. The boy is apparently in the best of health.

This case may safely be classed as a severe case of acute tetanus. Attempts to grow the specific organism from the necrotic tissue excised from the wound were not successful, but of the clinical identity of the disease there can be no doubt. It is not a case of the fulminant type of the disease, but from the severity of the symptoms and the rapidity of development after their appearance, it may without question be classed as a severe type, in which the mortality is great. Intraspinal injections of magnesium sulphate formed the principal part of the successful treatment. It is true that antitoxin was used over a prolonged period, but the administration of antitoxin after the appearance of symptoms has never been proved to be of any benefit, and its use in this instance was regarded merely as a possible aid, in which, however, no faith was had.

Of the value of the treatment by magnesium sulphate suggested by Meltzer, no one who witnessed this case has any doubt. A patient in violent spasm and continuous opisthotonos was repeatedly reduced to complete and lasting relaxation in the course of a few minutes by an intraspinal injection of magnesium sulphate; a result was thus achieved surely, promptly, and safely, which can be but weakly approximated by the usual sedatives, and even then after hours instead of minutes. Death in tetanus is said to be due, in one-half the cases, to asthenia produced by the excessive muscular

action and inability to take food, and in most of the remaining cases to asphyxia during a convulsion; inasmuch as we have in magnesium a means of blocking all motor impulses to the muscles, thereby preventing their action, it seems reasonable to suppose that the system, thus spared the enormous expenditure of energy incident to convulsions, may be able in some way to convert that energy into a means of protecting itself and may possibly even be aided in the production of a specific antitoxin. This, of course, is as yet pure speculation and has been repeatedly referred to; until we understand more of the formation of antitoxin by the body and of the action of the tetanus toxin it will remain speculative. It may be possible, as Blake suggests, that during this preliminary stage, before the body has formed its own antitoxin, the use of artificial antitoxin is of value; this likewise is problematical. Be the theory what it may, there seems no doubt that the use of magnesium is beneficial in tetanus; by its use it was possible to reduce this patient from a condition of violent muscular spasm to one of complete relaxation lasting from ten and one-half to twenty-nine hours, usually about twenty-four hours.

The chief danger in the use of intraspinal injections of magnesium lies in its direct depressing influence upon the respiratory centre; this effect was produced repeatedly. The first injection produced no apparent effect upon respiration, nor did the third injection, which consisted of a smaller dose and of less concentration than usual (2 c.c. of 16.6 per cent. solution), and was thus possibly too small to affect the respiratory centre. After each of the other injections, however, there was a more or less marked drop in respiratory rate, which was accompanied by a decrease and irregularity of amplitude; this change in respiration was of eleven to fourteen hours' duration and in some instances alarming, notably after the second and fourth injections, when the rate dropped to seven and five per minute respectively, necessitating constant watching and preparation for immediate artificial respiration. In spite of this respiratory collapse, however, the circulation remained in good condition; there was no cyanosis and the pulse remained regular and steady throughout. Each respiratory collapse was accompanied by a fall in pulse rate, the curve of which followed that of the respiration rather accurately. One must regret that no blood-pressure observations were made during those periods, inasmuch as it seems highly likely that there may have been a fall and that the pulse if followed accurately with regard to blood pressure would have shown a distinct drop. The actual drop in pulse rate is of interest, inasmuch as Meltzer states that "heart and pulse remain normal" in anesthesia achieved by intraspinal injection of magnesium. There was also an apparent decrease in effect upon respiratory rate with repeated administration of the same or increasing doses. In no instance did the patient's condition demand a second lumbar puncture to wash the salt out

of the canal, as recommended by Meltzer. As a precaution the head was elevated during and after the third and subsequent injections, in order to prevent the injected fluid from reaching directly the respiratory centre. The injection was frequently followed by a profuse secretion of mucus, at times severe enough to embarrass respiration, but apparently easily controlled with atropine. This condition is referred to by Logan<sup>3</sup> and others.

After each injection there followed promptly a paralysis of the legs, abdominal walls, sometimes the arms, while the neck and masseters usually escaped, and the muscles of the face practically always remained unaffected. This paralysis appeared within thirty to sixty minutes and varied in duration from eighteen to twenty-nine hours. Several instances have been reported in which perfect, although transient, use of muscles (legs) followed an injection; in only two instances did that occur in this case.

Owing to the uncertain mental condition of the child, due to the illness, any observations as to sensation and subjective state are scarcely trustworthy; it seems certain, however, that he was comatose for thirteen hours after the fourth injection and for fourteen hours after the fifth.

No constant effect of the injection of the magnesium upon temperature was shown. After the first, third, sixth, and eleventh injections there was a decided rise; the ninth injection had no effect, and a fall in temperature followed the remaining five injections. The only variation in temperature of any serious consequence occurred during the collapse after the tenth injection.

Retention of urine was the rule and it was necessary to catheterize the patient for nine days, August 20 to 29, that is, from the time of the fourth to the eleventh injection. Previous to that time he had been voiding urine frequently and in small amounts; he probably had a paradoxical incontinence. The bowels moved involuntarily throughout the illness; in how far this was due to the magnesium injections is, of course, a question. No purgative effect was noted from the magnesium absorbed.

In this case magnesium did not relax the masseters and pharyngeal muscles sufficiently to allow the patient to take nourishment throughout. From August 21 to August 30, that is, from the fifth until the last injection had been given, it was necessary to feed the boy by means of the stomach tube, which he bore very well. In addition, normal salt solution infusions were given repeatedly as well as salt enemas, which were retained. After the last injection small amounts of chloral and bromide were used for a few days.

Regarding the technique of lumbar puncture it may be said: our first punctures were made between the second and third lumbar vertebræ; this site soon became excoriated owing to too vigorous

cleansing and the subsequent punctures were made between the first and second lumbar vertebrae, the skin being cleansed simply with soap and water, alcohol, and ether. A varying amount of cerebrospinal fluid was withdrawn. An interesting and very important point, to which no reference has been found, is the change in the cerebrospinal fluid following the punctures: the second puncture was made twenty-one hours after the first and 25 c.c. of a very turbid, grayish fluid was withdrawn. The appearance of the fluid suggested meningitis, but no organisms were found in stained specimens and cultures remained sterile; it was subsequently learned that this finding is not infrequent after the injection of serum in meningitis and is due to the presence of white blood corpuscles in the cerebrospinal fluid. At subsequent punctures turbid fluid was usually found, but never in such large amount as at the second puncture.

The following is a brief abstract of the cases reported to date:

CASE I.—(Blake.) Male, aged fifteen years, seven days after a crushing injury of the left hand began to show stiffness of the jaw and neck. Upon admission to the hospital there was well-marked tetanus. Under nitrous oxide anesthesia, 40 c.c. of tetanus antitoxin was introduced into the cervical meninges, and 20 c.c. into the median cephalic vein. The following day 35 c.c. of antitoxin was injected into the lumbar meninges. This treatment was without avail. On the following day, that is, the third, 4.5 c.c. of a 25 per cent. solution of magnesium sulphate was injected into the lumbar meninges. Stiffness of the entire body disappeared in six hours and the patient took nourishment well. On the following day the convulsions returned and in thirty-three hours the effects of the injection had entirely disappeared. A second lumbar puncture was done, 8 c.c. of a 12.5 per cent. solution of magnesium sulphate was injected. A similar reaction followed; the spasm gradually returned, and the injection was repeated in twenty-nine hours. Five days later the last lumbar puncture was done, 12.5 per cent. solution being used. After this injection his muscular spasm never returned and his convalescence was without event.

CASE II.—(Blake.) Seven days after the reception of a wound of the leg the first symptoms of tetanus appeared. Extreme convulsions rapidly supervened. The patient upon admission to the hospital was immediately given 1.5 c.c. of a 25 per cent. solution of magnesium sulphate into the lumbar meninges. Within two hours he was somewhat relaxed. Slight convulsions, however, continued to occur and he died sixteen hours after the injection, which apparently was in no way to blame for the child's exitus. Autopsy revealed tetanus bacteremia. The case was apparently hopeless from the start.

CASE III.—(Logan.) Male, aged eleven years. An incubation period of nine days following a gunshot wound of the hand. Typical tetanus upon admission. Bromides and chloral were

given. On the following day general convulsions appeared together with opisthotonos. 4 c.c. of a 25 per cent. solution of magnesium sulphate was injected by lumbar puncture; 50 c.c. of antitoxin was injected into the sciatic nerves, brachial plexus, and the tissues around the wound. Complete relaxation occurred in forty-five minutes. Profuse bronchorrhœa occurred in four hours and forty minutes. The tonic spasms returned thirteen hours after the injection. A second injection was followed by complete muscular relaxation. Severe convulsions appeared two hours and fifteen minutes after the second injection and were due to the administration of an enema. Respiratory failure followed three hours after the injection, and the patient died seventeen hours after the injection from cardiac collapse, the pulse ceasing to beat before respiration stopped.

CASE IV.—(Logan.) Female, aged twenty-four years. Uncertain incubation following vaccination of the arm. Fulminant attack of severe tetanus for which two injections of 4 c.c. of a 25 per cent. solution of magnesium sulphate in the lumbar meninges were given, each without avail. Death followed shortly after the second injection. Apparently a hopeless case.

CASE V.—(Franke<sup>4</sup>.) Male, aged thirty-five years. Incubation period of twelve days. Typical though mild tetanus. Three injections, first of 1 c.c., then of 2 c.c., of 25 per cent. solution of magnesium sulphate into the lumbar meninges. Marked cessation of muscular spasm followed each injection. Voluntary motion returned and the patient took nourishment well. Complete recovery. In this instance muscular relaxation apparently lasted about thirty hours. The case was not severe.

CASE VI.—(Robinson<sup>4</sup>.) Male, aged eleven years. Uncertain incubation period. Typical tetanus of moderate grade. Immediate injection of 3 c.c. of 25 per cent. solution of magnesium sulphate. In two and one-half hours complete muscular relaxation, absence of knee-jerks. No return of opisthotonos. Complete return of rigidity within eighteen hours. Second injection 3.5 c.c. of 25 per cent. solution of magnesium sulphate. Complete muscular relaxation in one and three-quarter hours which lasted certainly more than ten hours. Third injection two days after the second, 4 c.c. of 25 per cent. solution injected into the lumbar meninges. In one hour complete absence of spasm; in two hours complete relaxation; in fifteen hours slight return of rigidity. From this time on slight rigidity, with decreasing tetanic symptoms. Patient discharged well in the course of two weeks.

CASE VII.—(Greeley<sup>4</sup>.) Male, aged two years. Uncertain incubation period. Apparently typical tetanus of moderate grade. Two subcutaneous infusions, each containing magnesium sulphate,

<sup>4</sup> Zentralbl. f. inn. Med., 1907, xxviii, 345.

<sup>4</sup> Jour. Amer. Med. Assoc., 1907, xlix, 493.

<sup>4</sup> Ibid., 940.

2 drams, were given on successive days. Complete subsidence of symptoms. Typical but apparently not a severe case.

CASE VIII.—(Greeley.) Male, aged forty-five years. Chronic tetanus. Incubation period of four weeks. Slight stiffness of neck and inability to open the mouth. Symptoms subsided completely after injection of 3 drams of magnesium sulphate solution subcutaneously. Apparently a very mild grade of chronic tetanus.

CASE IX.—(Lyon.<sup>7</sup>) Male, aged seven years. Incubation period of eight days. Moderately severe tetanic symptoms by the eleventh day. On the twelfth day 2 drams of magnesium sulphate was given under the skin in the abdomen. Muscles were markedly relaxed. On the following day injections were repeated for return of symptoms, and again on the second, fifth, and seventh days after the first injection. Apparently a complete cure.

CASE X.—(Henry.<sup>8</sup>) Male, aged nine years. Incubation period of three days. Severe typical tetanus upon admission. 3 c.c. of 25 per cent. solution of magnesium sulphate injected three times for muscular spasm, leading to complete relaxation in two hours. During the period between injections patient was comfortable, taking nourishment fairly well. Catheterization necessary. Result, cure.

CASE XI.—(Henry.) Male, aged nineteen years. Seven days' incubation. Severe tetanus with moderate opisthotonos on admission. Lumbar puncture. Injection of 6 c.c. of 25 per cent. solution of magnesium sulphate. Two and one-half hours patient in a deep sleep, difficult to arouse. On the following day rigidity was most pronounced. On the third day was as marked as upon admission, and upon the fourth day patient died, apparently in collapse.

CASE XII.—(Henry.) Male, aged nine years. Six days' incubation period. Severe tetanus upon admission. Injection of 2.5 c.c. of 25 per cent. solution of magnesium sulphate. Complete relaxation in two hours. Reappearance of rigidity in nine hours. Lumbar puncture again performed and injection of 2 c.c. of magnesium sulphate, without any result. Condition grew worse and patient died.

CASE XIII.—(Henry.) Male, aged forty-five years. Three weeks' incubation period. Slight trismus upon admission. The following day rigidity increased. Lumbar puncture was performed, and 6 c.c. of 25 per cent. solution of magnesium sulphate injected. Upon injection patient immediately complained of burning sensation up to the base of the skull and along the main nerve trunk. This severe pain lasted for fifteen minutes. Complete relaxation occurred in one hour; on the second day a similar injection was made with similar results. Following the second injection, however, the patient fell into a deep sleep, was completely relaxed, respiration

<sup>7</sup> Jour. Amer. Med. Assoc., 1908, 1, 1688.

<sup>8</sup> International Clinics, 1907, iv, 1.

became shallow, and temperature and pulse rising. The following day he remained dull and sleepy, came to an end unconsciously and died without any rigidity being present. The reporter says: "It is very much a question whether the magnesium sulphate did not contribute to the patient's death."

There are thus 14 cases on record treated with magnesium sulphate. Of 11 cases treated by subarachnoid injections 5 have recovered, a mortality of 55 per cent. This result is encouraging, inasmuch as almost all the cases in this series were of that type of tetanus which usually proves fatal; 3 cases were treated by infusion, none of them of severe type, and there were 3 recoveries.

In conclusion, it may be affirmed that by the use of magnesium sulphate it is possible to achieve complete muscular relaxation in almost all cases of tetanus; from the report of results there seems to be a distinct benefit to the patient in this condition, inasmuch as it prevents the rapid exhaustion due to convulsions and in most instances has made it possible for the patient to take nourishment. It may likewise be affirmed that, while as yet there is comparatively little clinical evidence upon which to base general statements, yet it seems possible to avoid the dangerous effects of an overdose of magnesium salts, and it is likely that when the technique has been worked out thoroughly the treatment will offer a possibility of saving a great many patients with tetanus who at the present time are given up as hopeless at first sight.

I desire to express my gratitude to Professor William S. Halsted for the privilege of reporting the case. For the fulness and accuracy of the clinical notes, I am indebted to Drs. J. H. Chesnutt and R. D. McClure.

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### **TRACTION IN THE TREATMENT OF HIP DISEASE.**

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If surgical clinics in different cities are visited one finds that there is great diversity in the manner of treating hip disease. If, however, the subject is examined more closely it will be found that the accepted principles of treatment do not vary greatly. Surgeons treating a chronic affection, with changing indications, may vary in their opinion as to which symptoms demand most attention, and in this way they may differ.



It is now generally admitted that radical operative interference in hip disease is not to be undertaken until other measures have failed; in this paper for the sake of brevity the subjects of excision, amputation, and erasion will not be considered. It is also universally believed that in combating hip disease (a tuberculous affection) as much fresh air and activity as is possible is of the greatest importance; no space will be devoted here to an exposition of the advantages of these essentials of treatment, nor of the necessity of proper nutrition.

The methods of treatment at present in general use may be grouped as follows: (1) The method with little reliance upon mechanical aids; (2) the method utilizing the Thomas splint; (3) that attempting a plaster-of-Paris fixation as the chief feature of conservative treatment; and (4) a method attributing much value to traction.

1. TREATMENT WITH LITTLE MECHANICAL AID. In neglected cases the course of the development of tuberculous coxitis is but little influenced by treatment. In the initial stage, and when little pain is present, the child may limp and avoid instinctively, or is prevented from making, violent motion of the joint; later, as the disease progresses and the tissues are more extensively involved, there may be much sensitiveness and pain, night cries from exaggerated muscular irritability, and distortion from tonic muscular spasm; finally, disorganization of the joint occurs, distruction of the head, and obliteration of the upper border of the acetabulum take place with the flexed and adducted position of the limb, firmly held "splinted" against the pelvis by stiffened muscles and contracted ligaments (Figs. 1 to 4). The acute pain, if present, ceases as the destructive osteitis becomes walled off or is supplanted by a constructive osteitis. The patient, confined, by pain or the sensitiveness of the limb on motion, to the bed or lounge, becomes able to move about, and needing crutches or a crutch on account of the distortion of the limb is able to go about with comparative freedom, and, eventually, in a large number of cases, is cured with a distorted limb. In a certain number of cases in which the process is considerable, the tuberculous detritus acts as an irritant; an abscess is developed, which may be absorbed and remain an encapsulated caseous mass, or may enlarge, force its way through the fascia and skin and evacuate itself, leaving a sinus which heals under normal conditions. Secondary infection of the tissues is, however, not infrequent, extending to the bone which becomes involved in infective osteomyelitis, which in a certain number of cases leads to extensive necrosis, chronic sepsis, amyloid disease of kidneys, and death or chronic invalidism. In a majority of cases immunity becomes established in time, and recovery takes place, leaving the patient in a more or less crippled condition.

As this process is one which lasts for years and is often characterized by alternate periods of improvement and relapse, it is not unnatural that those in charge of the nursing of the patient, seeing im-

provement follow any suggested remedy from the seton to faith cure, attribute such improvement to the applied remedy, while in reality recovery from the disease is not exceptional. The true measure of the success of a method of treatment is the amount of resulting deformity, rather than the fact of recovery from pain. Usually the child is kept in bed during the acute stage, with some arrangement for the correction of deformity. Crutches are given later to limit the weight bearing use of the limb as soon as locomotion is



FIG. 1.—Radiogram of a case of hip disease not treated by traction, showing deformity and pathological dislocation. (Bradford.)

possible. Later still, the patients are practically left to the curative process of Nature, protected from jars only by the occasional or intermittent use of canes or crutches.

Diseased bone may, in a short time, regain enough strength to bear slight strain without injury and without pain. The patient walks and is encouraged to walk by the fact of freedom from pain, but until the bone is restored to its normal strength, the danger of injury to tissue from violence, incident to ordinary activity, cannot

be avoided. Under this condition after slight bruises either a relapse occurs, or enough irritation is kept up to develop deformity. It is to these facts, that is, the occasional relapse and the gradual development of the deformity, which gives rise to the popular belief in the practical incurability of the affection. In the minds of many surgeons also without an extensive study of the course of the affection, through a long period of years and under many differing conditions and methods of treatment, an opinion becomes established that if the general health is maintained, mechanical treatment is of little importance.

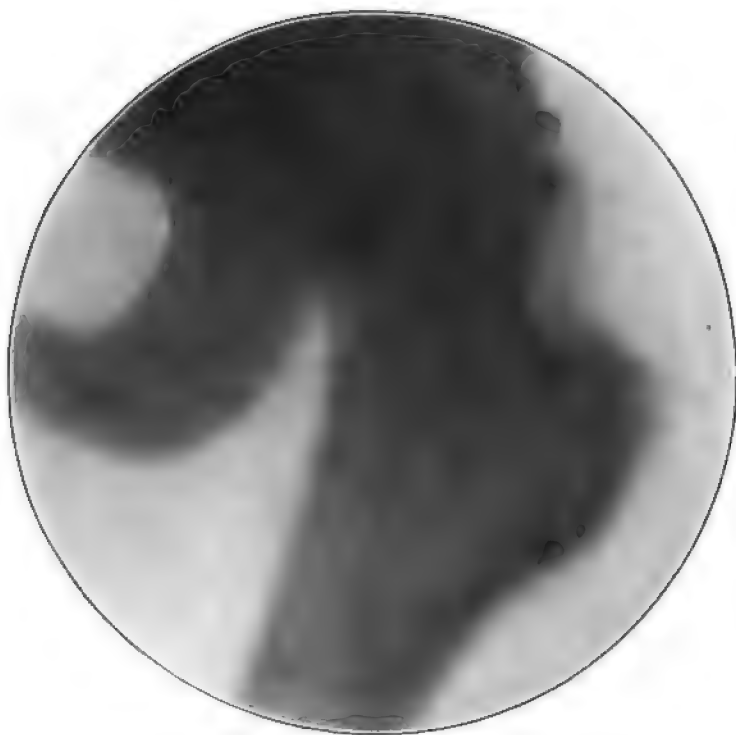


FIG. 2.—Radiogram of a case of hip disease (with abscess) twenty years after the cessation of treatment by thorough traction and protection. A strong, useful limb without deformity, with slight motion; photograph in Fig. 19. (Bradford.)

In fact, a large proportion of cases of imperfectly treated hip disease will recover eventually without treatment, but with deformity of greater or less severity; this ensues, in many cases, after years of suffering and the frequent occurrence of abscess and resulting sinuses, and not infrequently sepsis and septic osteomyelitis.

2. **THE THOMAS SPLINT.** The irksomeness of bed confinement, the "wire britches" (that is, the *gouttière de Bonnet*) employed by

the French surgeons, and the manifest need of some treatment for the disease, led to the introduction by Mr. Thomas, of Liverpool, of his excellent apparatus. It is somewhat singular that so admirable a contrivance as this should have found so little general acceptance in the surgical world. It is easily made, an efficient aid, inexpensive and requires a skill for adjustment no greater than can be acquired by anyone familiar with the use of appliances needed in the treatment of fractures. The advantages of the method have been often demonstrated, notably by Mr. Thomas himself, and at present by Mr. Jones, of Liverpool, and Dr. Ridlon, of Chicago; and, lately, in an excellent manner, by Dr. Bennie, of Australia; but they have not been as generally adopted by surgeons as the merits of the apparatus deserve.



FIG. 3.—Section of a hip-joint with hip disease, showing deformity and pathological dislocation. (Bradford.)

The chief reason why the Thomas splint has not met with general adoption is, in all probability, the simple one that surgeons avoid mechanical aids when possible. In the larger surgical clinics where patients are treated in great numbers, the operative demands are so great and the interest in operative methods is such, that little time and thought are given to the use of mechanisms. A mechanical appliance usually is left to juniors, or assistants, and is often imperfectly applied with unsatisfactory results. It is much easier to order the application of plaster-of-Paris, with which the student or assistant is usually familiar. In addition there are certain im-

perfections in the Thomas splint itself as an ideal appliance which prevents its enthusiastic acceptance by specialists.

It furnishes imperfect fixation, it does not prevent increased interarticular pressure, and it does not prevent the development of pathological dislocation. For larger patients it is an awkward appliance. It necessitates the use of crutches, and does not allow

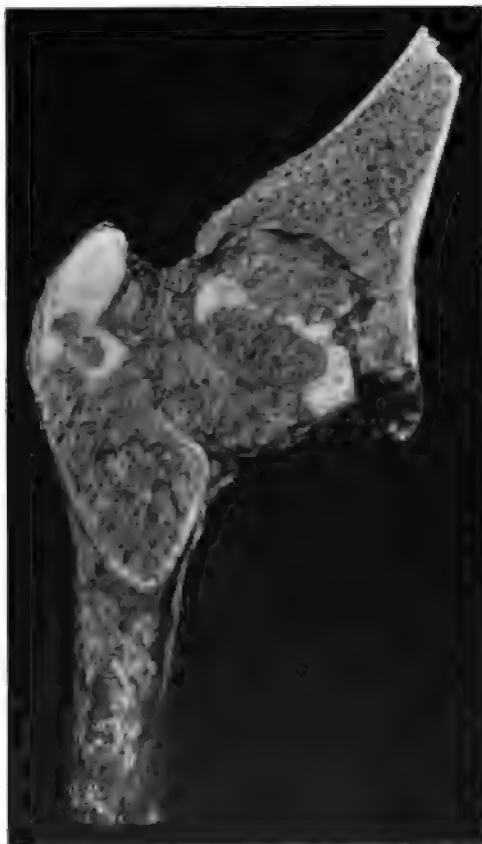


FIG. 4.—Section of a hip-joint after hip disease of a severe suppurating type. Death occurred from tuberculous meningitis three years after the patient had discarded traction treatment for hip disease: the limb was useful, and there was no deformity and no pathological dislocation at the hip. Traction had been applied efficiently for one year. (Bradford.)

the patient to sit with comfort. On the other hand, although some skill is demanded in its adjustment, this is not sufficient to prevent its ready use. It enables the patient to move or to be handled without discomfort except during the acutest stage, it diminishes or prevents flexion deformity, and it checks but does not prevent adduction. In double hip disease it is an admirable appliance. Mr. Thomas

himself made no extravagant claims for the appliance, stating that while hip disease could be cured probably as quickly without this splint, the care of the case was easier, and the patient suffered less, and there was less deformity than when it was not employed. The splint is more agreeable to patients than an efficient plaster bandage to the trunk and thigh.

3. PLASTER-OF-PARIS BANDAGES. A surgeon in charge of a large number of patients placed in an institution is obliged to devote his attention to the development of a method of treatment adapted to his nursing facilities. A well-applied plaster-of-Paris spica bandage, reaching from above the mammillary line to below the knee, placing the patient in a portable frame with facilities for moving the patient about freely, and an abundant supply of fresh air, combine to afford a method of treatment which is satisfactory during the acute stages of the affection, without a demand on a large nursing force. This is the treatment so successfully conducted at Berck sur Mer; but a short spica bandage, combined with crutches in common use in many clinics, as an ambulatory method of treatment of hip disease, cannot be recommended as a thorough method of treatment.

4. TRACTION APPLIANCES. The employment of traction, that is, a pull, in the treatment of hip disease is one which is naturally suggested by the distorted position of the limb and the muscular spasm which evidently crowds the head of the femur into the acetabulum, increasing the destructive osteitis in the direction of the pressure, aggravating the disease, and increasing the deformity. As extravagant claims, however, were at first made of the benefits to be derived from traction as the chief principle of treatment in hip disease; as expensive, elaborate appliances requiring special skill in adjustment, and much care in nursing have often been recommended in the treatment of hip disease, it is natural that the method of treatment be regarded with doubt. The active surgeon not without reason looks upon an expensive, complicated apparatus, needing special training for adjustment, as unsuited for general use. That, however, the principles of the judicious employment of traction in hip disease are sound, and that they have in practice been applied with great benefit has been abundantly shown. The method merits the careful attention of surgeons.

Although it is possible to classify the methods of treatment of hip disease in groups, in actual practice the treatment of hip disease varies greatly—from that which confines the patient for years to a couch, to attempts at “motion without friction” (as it is termed) of hips treated by splints, or to locomotion at will with the expectation that the application of a plaster-of-Paris spica will help the cure of the disease. In this maze of inconsistency, treatment should follow the clue furnished by pathological evidence which clearly indicates the advantage of the prevention of bone crowding.

If traction is applied to a normal adult hip, it will be found at

first to have no appreciable effect in distraction, that is, in drawing the head of the femur from the acetabulum, even if a considerable force or pull is applied—thirty pounds. The first effect is probably to stimulate the action of the powerful hip muscles so that the hip is held even more firmly than before. This has led some observers to infer that traction has no influence in drawing the head of the femur away from the acetabulum. If, however, a pull is applied to a diseased hip when the cotyloid ligament and the zona orbicularis are disorganized by the inflammatory process involving the capsule, it will be seen that even with a moderate pull of six pounds a marked distraction can be effected. This is demonstrated if a diseased joint is incised and the finger is inserted into the joint. It can also be shown by careful measurements of the length of a limb with a diseased hip, when a patient has been subjected to a traction pull for a few days. If any further proof is needed it will be furnished by a skiagram of a tuberculous hip-joint subjected to efficient traction. It will be seen that it is possible to draw a diseased femoral head away from the acetabulum, meeting a manifest indication to promote the healing of a joint surface affected with osteitis, and especially a hip-joint. If, in a given case even when there is little pathological relaxation of the capsule, a traction force is applied for a sufficient length of time, it will be found that a distracting effect will, in time, be accomplished. There is no doubt, therefore, that the surgeon has at his command a means of promoting healing by separating the diseased surfaces in hip disease under certain conditions.

If it is desired to immobilize the hip-joint absolutely, the difficulty of the attempt will at once be seen. Every motion of the trunk or of either extremity is transmitted to the pelvis which forms a part of the hip-joint. The futility of an attempt at exact fixation by securing the affected limb with a heavy plaster bandage, leaving the other limb free, is apparent; neither is absolute hip fixation secured by encasing the trunk with a plaster-of-Paris bandage, as it is impossible to prevent by means of a bandage the movements of the lumbar spine, or by compression upon the ribs to hold the upper portion of the trunk from motion. Furthermore, firm pressure upon the ribs prevents respiration and is impracticable. For absolute fixation it is necessary to hold firmly the whole trunk and both lower extremities. This is shown if an attempt is made to take a skiagraphic picture of a hip-joint when the patient moves the trunk.

The problem may be likened to that which would be presented if it were desired to prevent a snake from wriggling. This could be more readily done if the head of the snake were held and firm traction put upon the tail, than if the snake were placed within a glass tube. A rope made taut resists side pressure better than a slack one. Traction experiments upon a cadaver, using an efficient traction splint, made by my colleague, Dr. A. Thorndike, as well as

upon patients, demonstrated what has already been shown by Judson and others, that traction properly applied furnishes the best method of fixation to hip-joints. If the theoretical advantages of traction are accepted it should follow that practically when traction is properly applied better results should be secured than when this method is not employed (Figs. 5 to 9).



FIG. 5.—Illustrating the force of muscular contractions of the muscles controlling the hip. The weight is twelve pounds. Elastic bands are placed at the origin and insertion of each muscle, one band only for each muscle. (Bradford.)

In this connection the statistics of hip disease at the Boston Children's Hospital are of interest. Treatment, during the last thirty years, has included some form of effective traction during the acute and subacute stages of the disease, although all other known



methods of treatment have been thoroughly tried. The cases are treated largely in the out-patient department (with traction or protection splints), except in the more acute stage or when operative interference is needed. Those suffering from abscesses or in the

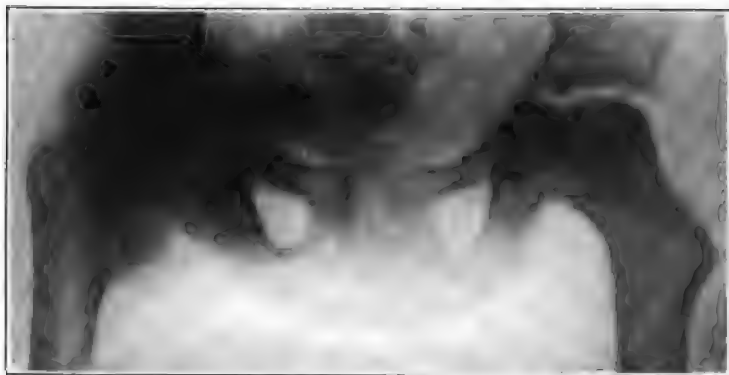


FIG. 6.—Radiogram of hip disease without traction. (Bradford.)



FIG. 7.—Radiogram of hip disease with ten pounds' traction. (Bradford.)

more severe or acute stages are referred to the in-service. A country convalescent home, seashore homes, district nursing, and a school for crippled children aid in the continued care of the patients.

The number of cases recorded and treated for hip diseases in the out-patient service, between the years 1883 and 1907, was 1809. Of these 983 were subsequently admitted as in-patients at the hos-

pital, representing the severer cases, and among these 502 were suppurative cases, that is, 30 per cent.

The operations other than incision of abscesses performed were as follows: between the years 1879 and 1907, 1154 cases: Amputations (at the hip-joint), 2; 1 surviving twenty years later and 1 death. Excision (including the cases subsequently amputated), 64; 9 deaths, 9 per cent. In addition to these a number of arthroplasties, curetting of the femoral head and neck, channelling of the neck, and 4 cases of dislocation of the head by incision in acetabular disease—with apparent relief. The general mortality of cases in the in-service is as follows, from the years 1895 to 1908: 606 cases of hip disease, 25 deaths, that is, 4 per cent. The causes of death were:



FIG. 8.--Amputation at the hip-joint at the age of eight years for hip disease, with extensive caries of the ilium. The amputation removed irritating pressure. The periosteum around the femur was saved in the flap. (Bradford.)

12 tuberculous meningitis; 1 empyema; 1 double hip disease; 1 hip disease and caries of the spine; 1 scarlet fever; 1 diphtheria; 1 after excision; 1 after abdominal incision for acetabular drainage; 6 from uncomplicated hip disease; total, 25. The mortality for uncomplicated hip disease was 1 per cent.

Of the 1809 recorded cases in the out-patient department, 144 are noted as having sinuses. This may be taken to indicate that in a majority of the cases with abscesses incised in the in-service there was little recurrence.

In order to determine more accurately the ultimate results, after a number of years, obtained by treatment, upward of four hundred postal cards were addressed to patients whose records showed that the affection was of sufficient severity to demand attendance at the

out-patient service for a year or more, but no patient was communicated with who was admitted after the year 1899 (the inquiry being made in January, 1908).



FIG. 9.—Radiogram and portrait of the same patient shown in Fig. 8 twenty years later. From the periosteum bone growth developed, enabling the patient to wear an artificial leg and aiding him to lead an active business life. (Bradford.)

One hundred and sixty-seven replies were received, stating that of these 9 had died from the complications following hip disease; 2 of these had recovered from the affection of the hip, but had died, 1 from an operation for appendicitis and the other from some dis-

ease not stated, unconnected with the disease of the hip, and after he had recovered from this; that is, a mortality of 6 per cent. approximately. 32 reported their ability to walk without limp; 46 with slight limp; 52 with limp the amount not stated; 5 with a bad limp; 1 required an apparatus and crutch; 1 required a crutch. All reported their ability to work or attend school; none were bed ridden or disabled, with the exception of those requiring crutches. On further investigation more full replies were received from 98 of the 167 patients.

The amount of shortening was reported to be, none in 12; one inch and under in 26; between one and two inches in 28; between two and three inches in 11; between three and four inches in 10; over four inches in 8; in 3 the shortening was stated as slight, but the amount was not given; that is, in nearly 70 per cent. the shortening was under two inches; 35 had had abscesses; 5 had discharging sinuses; that is, 37 per cent. suppurating cases.

A personal examination was made of as many of these latter cases as could be seen, with the following results: 26 were found to be non-suppurating cases (that is, had never had an abscess); 25 were cases previously suffering from abscesses and sinuses; in none were any unhealed sinuses. Of the 26 non-suppurative cases: In 11 the motion was perfect (that is, 90 degrees or over); in 7 there was slight motion (under 10 degrees); in 8 there was no motion. There was deformity of flexion in 11 as follows: 1 of 10 degrees; 2 of 15 degrees; 1 of 25 degrees; 1 of 30 degrees; 1 of 40 degrees; 3 of 45 degrees; 1 of 50 degrees; 1 had abduction of 40 degrees after Gant's operation. There was deformity of adduction in 8 as follows: 1 of 10 degrees; 2 of 20 degrees; 1 of 25 degrees; 2 of 30 degrees; 1 of 40 degrees; 1 of 45 degrees. There was no pathological dislocation in 19, the trochanter being below the Nélaton line. In 3 the trochanter was one-half inch above the line; in 1 was one inch; in 1 was one and one-half inches; in 1 was two inches; in 1 was three inches. In the 25 suppurative cases (that is, with previous abscess), there was stiffness at the hip-joint in 11; slight motion in 7; good motion in 2 (20 degrees to 30 degrees); perfect motion (90 degrees or over) in 5. There was a permanent flexion deformity in 15 as follows: 4 with 10 degrees; 2 with 15 degrees; 2 with 20 degrees; 1 with 25 degrees; 1 with 40 degrees; 2 with 45 degrees; 1 with 55 degrees; 2 with 60 degrees. In 2 there was abduction: 1 of 10 degrees, and 1 of 20 degrees. In 12 there was adduction as follows: 5 of 10 degrees; 1 of 15 degrees; 1 of 30 degrees; 1 of 40 degrees; 2 of 45 degrees; 2 of 50 degrees. In 12 there was no pathological dislocation, the trochanter not being above Nélaton's line. In 1 the trochanter was one-half inch above the line; in 3 was one inch; in 3 was one and one-half inches; in 2 was two inches; in 1 was two and one-half inches; in 1 was three and one-half inches. In 1, a case of excision, there was no deformity, a strong useful leg, but three inches

shortening. No correction of deformity was made in these cases with the exception of 1, on whom a Gant operation had been performed. None of the patients needed crutches or apparatus. All walked about freely, any desirable distance. The results can be summarized as follows: It was found that the ultimate mortality was 6 per cent. For the cases under treatment in the hospital the mortality was 4 per cent. The percentage of abscesses for the cases under treatment was 30 to 37 per cent. The ultimate results showed useful limbs in 98 per cent. Shortening of less than two inches in 70 per cent. of the non-suppurative cases; perfect motion, 90 degrees or over, in 40 per cent. of the non-suppurative cases; absence of flexion deformity in 60 per cent., and absence of pathological dislocation in 70 per cent.

In the suppurative cases there was perfect motion in 20 per cent. In free flexion there was good motion (20 per cent.) in 10 per cent. of the cases. There was absence of deformity in 40 per cent. There was absence of pathological dislocation in 40 per cent.

To estimate the value of these results a comparison should be made with the results recorded in other institutions and under other treatments. It should be borne in mind that the statistics of the Boston Children's Hospital are not taken from selected cases or cases placed under favorable circumstances. Many of them were neglected cases with existing deformity and pathological changes when treatment was first undertaken at the Children's Hospital. Pains were taken to verify the diagnoses in the cases by the recorded testimony of competent observers through a sufficiently long period, and doubtful cases were rejected; but otherwise the cases represent those presenting themselves at a charitable hospital from the poorer class in a large American city. In the worst cases they received the benefit of a stay in a convalescent home for a time, but the greater part of the treatment was under home care.

The recent report of the results from treatment, by means of a plaster-of-Paris spica bandage with crutches, of a number of cases at a seaside home, may be used in comparison.<sup>1</sup>

These cases were at a seaside home and the observations were upon cases two years after the beginning of treatment, ages four to fifteen years. The treatment consisted of a plaster-of-Paris bandage applied from the mammillary line to below the knee, worn constantly for four or five months, crutches and an elevated shoe on the well foot being furnished. This was followed by a plaster bandage which allowed freedom at the knee and later by a lighter appliance. The children, even with an elevated shoe, constantly laid aside their crutches, allowing the full weight to fall in walking or at play upon the diseased hips.

In 100 cases, 3 with double hip disease, there were 69 with ab-

<sup>1</sup> Sindling Larsen, *Nordeiskt. Med. Archiv*, 1905-1906.

scesses; 99 cases were treated conservatively, but in 29 of them it was found necessary to excise the hip; in 4 cases excision was performed at once. The ultimate functional result of the cases or mortality is not given, but the high abscess rate and the large percentage of resection is noteworthy. The mortality of hip disease in the German Surgical Clinics, according to the statistics published by Dollinger<sup>2</sup> from various surgical clinics is as follows: In suppurative cases, 27 per cent. were cured; 24 per cent. were not cured; 48.8 per cent. died. In non-suppurative cases the mortality was 16.5 per cent.

Cazin reported a mortality in 80 suppurative cases at the sea-coast hospital, of Berck sur Mer, of 12.5 per cent.; 55 per cent. were cured. Menard<sup>3</sup> at the same institution recently reports even better figures: 1321 cases both suppurative and non-suppurative; 95 deaths, 54 in cases not operated upon; 41 in cases operated upon (that is, excision), 7 per cent.

The treatment at Berck is at present chiefly recumbent treatment, with plaster-of-Paris bandages, fixation, and largely out-door exposure in the day time on a portable frame.

The chief cause of death was tuberculous meningitis, 1 out of 56. Tuberculous meningitis was as common in cases operated upon as in cases not operated upon. The deaths from hip disease proper, that is, when other tissues were not involved, were few.

Mortality statistics quoted by Whitman<sup>4</sup> are as follows: At Tübingen, 40 per cent.; Kiel, 48.59 per cent. non-operative cases, 53.96 per cent. operative; at Marburg, 35 per cent. non-operative cases, 40.4 per cent. operative cases; at Heidelberg, 46.6 per cent. non-operative cases, 58 per cent. operative cases; in Zurich, 37.7 per cent. non-operative cases, 54 per cent. operative cases; in Vienna, 17 per cent. in all cases; in Göttingen a mortality of 40 per cent. Rabi reports a mortality of 20 per cent. in a large number of cases, some of which, 14 per cent., were still under treatment. At the Alexandra Hospital, in London, the mortality was 26 per cent.

Statistics of the ultimate functional results may be quoted as follows: Dollinger: in 14 cases, 2 walked with an excellent gait, 3 fairly well, 3 limping badly, 1 requiring cane and apparatus, 1 requiring cane, 1 with a slight limp, 1 in a poor condition, and 1 bed ridden. The average shortening from 4 to 8 cm. There was pathological dislocation in all. On the average the trochanter was 2 to 3 cm. above Nélaton's line, in several cases as much as 6 cm. No mention is made of motion, or of absence of deformity. The usual percentage of abscesses in hip disease is estimated as 50 per cent. by Whitman.

<sup>2</sup> Joachimsthal's Handbuch.

<sup>3</sup> Étude sur coxalgie, Paris, 1907.

<sup>4</sup> Treatise on Orthopedic Surgery, third edition, p. 391.

It appears, therefore, that as far as can be judged by statistics, the traction treatment employed at the Boston Children's Hospital is justified by superior results. If these figures showing the superiority of the results obtained in cases in which efficient traction is employed as a principle of treatment, as compared with those in which traction is not used, are not sufficiently convincing, further evidence can be offered in the figures collected by V. P. Gibney<sup>5</sup> at the Hospital of Ruptured and Crippled, New York. In the first series, 80 cases without mechanical or operative treatment, there was deformity in almost all cases. In 107 cases treated by mechanical means, not always efficiently, there was recovery without marked flexion. The mortality in Dr. Gibney's service, 288 cases, was 12 per cent. The mortality in the clinics of American cities is reported by Whitman as 12.5 per cent.

It should not be assumed that the results obtained by traction at a large civic hospital, treating largely the poorer classes with imperfect home nursing, indicate what can be accomplished if this principle of treatment is more thoroughly applied. Aseptic surgery is often imperfectly conducted in a crowded dispensary, but the results obtained are enough better than those obtained if all attempts at asepsis were discarded, to make all attempts to prevent sepsis obligatory. It is also true that better results in the treatment of hip disease are gained if the principle of traction is recognized than if it is ignored, even if the application is not as thoroughly or constantly applied as is desired. If the muscular force crowding the head of the femur into the acetabulum be estimated in a given case as a pressure of fifteen pounds and a distracting force of five pounds is applied for the greater part of the time, it may be sufficient to prevent the complete distraction of the femur and of the acetabulum and dislocation. The less pull, and the less constantly it is applied, the poorer the results. When bone destruction has already taken place in neglected cases, the results are not so good as those followed more carefully from the first. Among intelligent people and the well-to-do, with the best nursing facilities, better results are obtained in chronic cases.

Experience has justified the expectation of perfect recovery after thorough treatment, if this is undertaken before the disease has disorganized the tissue to a considerable extent. This expectation is justified in pulmonary consumption, and it is equally true in hip disease. In coxitis there is, however, the advantage for the surgeon that he has directly under his control the means of checking the irritating causes which delay cicatrization of the tuberculous tissue.

This belief is supported by the results obtained by the late C. F.

<sup>5</sup> Med. Record, March 2, 1878.

Taylor,<sup>6</sup> of New York. 94 cases, of which 24 were suppurative cases, of these 17 recovered with ample motion (82 degrees to 18 degrees); in 14 cases perfectly useful limbs thoroughly healed; in 5 the limbs were useful, but sinuses remained; 2 died. Satisfactory recovery occurred in the non-suppurative cases, except in 1 who was killed in an accident after having been run over. L. A. Sayre<sup>7</sup> also reported admirable results in the treatment of his private cases.

The following cases coming under personal observation may be of interest illustrating the value of traction in cases in which the final observations were made several years after the end of treatment:

CASE I.—C., a girl, aged eight years, treated in Paris by recumbency in a gouttiere de Bonnet for left hip disease for six months; later, in 1877, came under the care of the late Dr. C. F. Taylor, of New York. At this time the patient was suffering from pain and sensitiveness. Traction was applied by Dr. Taylor with much thoroughness for a period of a year and a half. A large abscess developed in the upper part of the thigh; it evacuated itself. The patient wore a convalescent splint for several years. She was seen in 1903, over twenty years after the cessation of treatment, and was found to be in perfect health; there had been no sinus subsequent to the healing of the abscess twenty-two years before. Motion in flexion was over 90 degrees; abduction 30 degrees. The limb was strong, useful, and undistorted; the trochanter was below the Roser Nélaton's line. As an evidence of the extent of the early epiphyseal disease there was a shortening from arrest of growth of the femur of one and one-half inches. The patient was a healthy married woman.

CASE II.—G., a boy, at the age of six years, in 1884, was seized with right tuberculous coxitis of a severe type while living in Paris. He was treated by portable recumbency, at gouttiere de Bonnet, for two years; afterward ambulatory treatment was gradually permitted and encouraged, followed by massage and electricity. At the age of twenty-one years, that is, in 1899, he returned to America with a thoroughly cured hip, but with bad deformity. There had been no abscess, but ankylosis in a faulty position had occurred with flexion of the thigh at nearly 90 degrees and 30 degrees adduction. There was marked pathological dislocation. The head of the trochanter was from two to three inches above Nélaton's line. The patient walked with a disfiguring limp. A subtrochanteric osteotomy with fixation in a strongly abducted position was performed with success, giving a useful limb and but little disfigurement of gait.

CASE III.—O., a girl, at the age of five years, in 1879 developed tuberculous osteitis of the left hip of a severe type. She was treated

<sup>6</sup> Mechanical Treatment of Disease of the Hip-joint, Boston Med. and Surg. Jour., March 6, 1879.

<sup>7</sup> New York Med. Jour., April 30, 1892.



from the first by means of traction, at first temporarily with recumbency, later with an ambulatory traction splint. An abscess developed and evacuated itself, leaving a sinus. Three years following the disease of the left hip the patient was attacked by a similar process in the right hip. Traction was no longer necessary on the left hip and the child was placed upon a double Thomas splint with abduction of both hips with a weight and pulley traction on the right. The child was at this time taken to Switzerland and remained abroad for several years. The traction on the right hip was discontinued and the child was carried about on a mattress in a light basket. An abscess developed in the right hip and sinuses in both hips discharged for some time but finally healed. In 1900 the patient was examined; there was a flexion deformity of both hips to an angle of 90 degrees; no adduction. Both sinuses had healed; 10 degrees of motion in flexion was present in the left hip and no pathological dislocation; in the right hip no motion was present and there was marked pathological dislocation. The patient was able to walk about freely and subsequently married and later gave birth to a healthy child.

CASE IV.—D., a boy, aged seven years, in 1880, developed severe disease of the right hip; severe night cries were prominent early symptoms. He was placed under efficient treatment, including traction with recumbency at first and later ambulatory treatment with traction. The case was a suppurative one; an abscess formed and evacuated itself, leaving a sinus which persisted for years and finally healed. A traction splint was worn for two or more years, but a convalescent splint was not worn constantly and a permanent flexion deformity of 45 degrees with adduction of 30 degrees developed gradually. This was corrected by means of a subtrochanteric osteotomy. Fixation in an abducted position was performed in 1905 with excellent result. On examination at this time there was stiffness at the hip-joint, but no pathological dislocation.

CASE V.—L., a girl, aged four years, in 1882, developed left hip disease without severe symptoms. Ambulatory traction treatment was carried out with thoroughness for three years. The patient was cured, was examined twenty-one years later and was found to have recovered with nearly normal motion of flexion, slightly restricted abduction, no pathological dislocation, a perfectly useful limb, but with an arrest of growth of the femur and a shortening of one and one-half inches.

As cases under exceptional care do not furnish a good basis for statistical comparison, I have not attempted to obtain the ultimate results in a large number of the cases treated outside of hospital practice in an experience in orthopedic practice of thirty years, and no statistics of those cases are offered. I wish, however, after a careful trial, without bias, of all methods of treatment, both operative and conservative, to record my conviction of the

great superiority of the conservative method in tuberculosis of hip-joint; of the great advantage of traction applied during the more acute stage to the point of distraction of the bones of the joint; and of the importance of protecting the joint from ambulatory jar for some time following the subsidence of all acute symptoms. There are three obstacles to the satisfactory cure of hip disease: (1) Tuberculous meningitis, best combated by fresh air and activity; (2) septic infection, best avoided by delaying operative interference; and (3) deformity, best avoided by proper mechanical treatment including, as of great importance, traction.



FIG. 10

FIG. 10.--Child wearing the abduction traction hip splint. (Bradford.)



FIG. 11

FIG. 11.--Rear view of the abduction traction splint applied. (Bradford.)

A valid objection to the employment of traction splints is that they are elaborate and expensive, and require special skill in nursing, beyond the reach of the general practitioner. The justice of this criticism has been so evident that many attempts have been made to simplify the apparatus needed for the efficient application of traction. It is thought that the traction splint in use at the Children's Hospital for the last three years is an improvement both in efficiency and simplicity on appliances of the sort similarly employed for the purpose of traction.

The accompanying illustrations (Figs. 10, 11, 12, 13, 14, 15, and 16) indicate the nature of this apparatus. It can be said to be but little more complicated than the well-known Thomas knee-splint, which it resembles, with the additional attachment of a perineal half-ring pressing to the well side and determining the amount of abduction, and a windlass attachment furnishing traction. The apparatus has the advantage that it does not need constant watching of the perineal straps, and that there is less chafing at the perineum

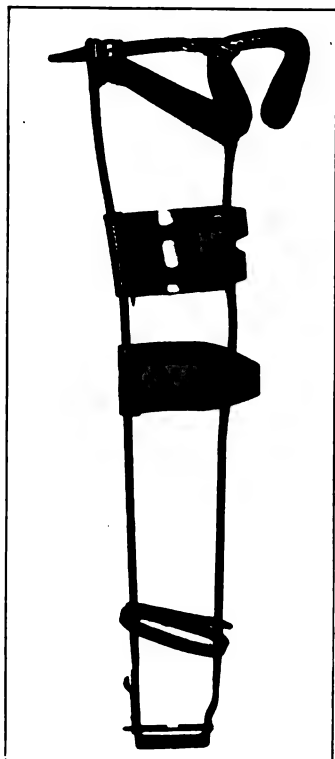


FIG. 12

FIG. 12.—Abduction traction splint padded. (Bradford.)

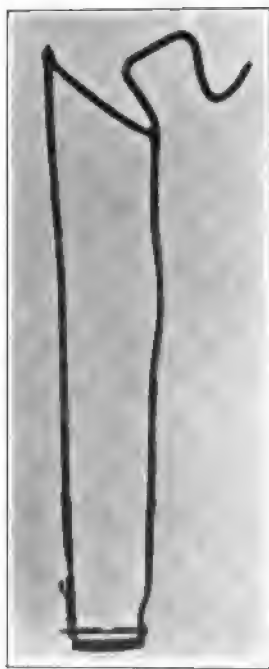


FIG. 13

FIG. 13.—Abduction traction splint without padding or straps. (Bradford.)

than when straps are used. It requires no skilled nursing. The cost of the appliance is not great and it can be readily made by any skilled blacksmith. Other forms of traction have been used and attempts have been made to simplify the windlass traction attachment; the substitution of buckles and straps has frequently been tried, but the requisite gradation of pull is not well furnished by a buckle and strap attachment. A simple spindle with a drop-ring catch can be made to answer in the place of the one used in the

Children's Hospital, although the latter will be found more convenient and but slightly more expensive. If it is remembered that when traction is needed in the acuter stages some delicacy of adjustment is needed to avoid increasing muscular spasm, the difficulty of using



FIG. 14.—Curve of the wire of the upper rings of the abduction traction splint. (Bradford.)

buckle and strap traction satisfactorily will be seen. In fact it may be said that no conclusion as to the results to be obtained from the traction treatment in the acute stage can be drawn when buckle and strap traction is employed. With the abduction perineal rings properly



FIG. 15.—Experiment showing the amount of fixation of the hip-joint from traction, with a strong pull endurable by the patient; no motion at the fractured hip-joint; the pelvis sways with movement of the leg, with the traction reduced one-half; motion of only 15 degrees in abduction and 7 per cent. flexion was possible. The less the pull the more the motion. (Bradford.)

adjusted, there is no soiling the splints which are not removed when the patient uses the closet. When the stage of the affection is reached where traction is not needed, the apparatus can be used simply as a perineal crutch, the traction attachment being discarded with or without the removal of the abduction addition. The splint is prevented

from slipping off by a strap passing over the shoulder, as in the Thomas knee-splint.

In the early stage crutches are furnished as an additional aid in locomotion, but they may be discarded at the will of the patient.

It is manifest that traction is only needed during a certain stage of hip disease, namely, the stage when there is exaggerated muscular spasm, which can be estimated by palpation of the adductor muscles, which in the more acute stages are in a state of spasm. As has been stated, during the acuter stages, it is desirable that the patient



FIG. 16.—Showing the amount of plaster-of-Paris spica fixation. A motion of 15 degrees in abduction and 10 degrees' flexion is possible at the hip-joint, when the bandage is carried to the mammillary line. (Bradford.)

be kept in a recumbent position and prevented from the trauma of jar or twist, including exaggerated muscular pressure. This is done by means of the traction splint indicated, but it can also be accomplished by the application of a weight and pulley. This, however, requires for satisfactory efficiency the fixation of the patient upon a frame in addition to the weight pull. Weight pull should only be used temporarily.

The importance of protecting the joint from jar during the convalescent stage is theoretically clear, but is often neglected in practice

for the reason that the patients suffer no pain and desire to be freed from all encumbrances, both crutches or splints. An irritation or weakness persists, due to occasional traumatism, in the partially recovered joint, which promotes the later development of deformity, that is, flexion and adduction (Figs. 17, 18, 19, and 20).

The two following cases serve to illustrate the value of splint protection of the hip:



FIG. 17



FIG. 18

FIG. 17.—Hip disease cured with traction treatment. Treatment was begun before there was extensive bone destruction. (Bradford.)

FIG. 18.—Same as Fig. 17, showing the range of motion. (Bradford.)

CASE VI.—A young man, aged twenty-two years, was seized with severe disease of the right hip while a student at the medical school. With the aid of crutches and a traction splint he was able to continue his studies after six months' interruption. Traction after a year became unnecessary to relieve symptoms. He was bebarred from hospital service by crutches and needed as he learned from experience some form of protection from the jar of locomotion. With a hinged ischiatic crutch he was able to enter upon arduous hospital duties and the hard work of early practice. His perineal crutch, uncomfortable on account of weight, was gradually discarded, but was for years needed to check the body jar of active loco-

motion. Recovery without deformity, with no dislocation, with slight hip motion, and a strong limb, followed.

CASE VII.—H., a man, aged twenty-four years, had suffered from hip disease since he was ten years of age and had recovered to the extent that he was able to walk about with crutches; was free from pain, but had several sinuses. He was, however, dependent upon crutches and was therefore debarred from a bread-winning occupation. He was furnished with a hinged ischiatic crutch, which was fitted with some difficulty, but finally made comfortable and worn

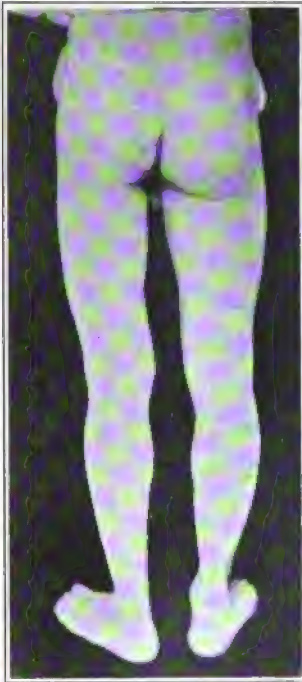


FIG. 19



FIG. 20

FIG. 19.—Cured hip disease—twenty years after the cessation of treatment. Fig. 2 shows skiagram of this patient; there is one inch shortening, but no deformity. (Bradford.)

FIG. 20.—Cured hip disease—twelve years after the cessation of traction treatment. A strong, useful limb without deformity. (Bradford.)

for six years as a necessary means of locomotion without which walking for any time was followed by pain and cramps. He was able to secure an important position of trust requiring activity. He subsequently was able to discard his appliance and remained in good health enjoying active usefulness and dying at the age of forty years of an acute disease.

CONCLUSIONS. It may be said that the surgeon has within his control several methods of treatment for hip disease. He can aid in the protection of the joint simply by the use of crutches,

he can aid in furnishing the patient facilities for increased activity and fresh air—the antidote to tuberculosis. He can, if he desires, prevent deformity and limit, if not prevent, bone destruction by exaggerated bone pressure, thereby checking the process and promoting bone healing.

The test of his success in treatment will not be the recovery of the patient, but the amount of resulting deformity. The aim of the surgeon in the treatment of any case without existing bone distortion should be a cure without distortion or disability. The elevation of the trochanter above the Nélaton line, adduction, abduction, or flexion, indicate that the surgeon either undertook the case too late to secure the best possible results, or that he was unable to apply thoroughly the methods of relief at his command (Figs. 19 and 20).

Traction can be employed without using expensive or elaborate apparatus; it does not demand unusual skill in nursing or from the surgeon, or more attention in the direction of the case than is within ordinary possibilities.

It can be claimed: That traction meets a pathological indication during the acute stage, that is, the stage of muscular spasm; that when used it should be applied with the purpose of furnishing distraction, that is, checking undue bone crowding; that when efficiently applied it furnishes a satisfactory measure of fixation of the joint; and that when traction is employed better results are obtained than when it is not made use of during the course of treatment of hip disease.

Patients with hip disease placed under favorable conditions recover; the death rate is low; there is no malignancy in the disease. Besides fresh air and proper nutrition, protection from jar and joint crowding are to be reckoned among the favorable conditions.

When traction is employed at an early stage and during the more acute period in a large number of cases, fewer abscesses will occur and these will heal more readily; better functional results are obtained, and a greater number of useful limbs; there is less deformity; pathological dislocation can be prevented in more cases; more cases recover with serviceable motion—than when the employment of traction is ignored or applied imperfectly.



## THE HEART IN PULMONARY TUBERCULOSIS.

### I.—THE HEART ITSELF NOT DISEASED.

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THE study of the heart in pulmonary tuberculosis will always remain a subject of the greatest importance and interest, as it yields information of great value in regard to diagnosis, prognosis, and treatment. The subject naturally divides itself into two sections, according as to whether or not the heart itself is diseased. In this paper that section will be discussed which deals with the heart itself not diseased, while a later paper will take up the second section, which has to do with disease of the heart as well as of the lungs.

Under this division the following points will be taken up: (1) The position of the heart; (2) the size of the heart; (3) dilatation, mentioning briefly the area of cardiac dullness; (4) auscultatory phenomena; (5) the pulse, mentioning briefly blood pressure; and (6) palpitation.

**THE POSITION OF THE HEART.** The position of the heart in patients with pulmonary tuberculosis depends directly upon the pathological changes that have taken place in the lungs. In the incipient stages the heart is rarely appreciably displaced, but in many patients in moderately and far-advanced stages the ordinary methods of exploration show some change in the position of the heart. In a clinical study of 2344 tuberculous cases at the Phipps Institute<sup>1</sup> the heart was said to be displaced in only 57 instances, 2.4 per cent.; on the other hand, Pottenger<sup>2</sup> thinks it is exceptional to find the heart in its normal position in advanced chronic tuberculosis. Adhesions often prevent the dislocation of the heart when we are led to expect it.

It is readily seen that the displacement of the heart may be much more pronounced when the right lung is affected, for the displacement is most often associated with contraction of one lung. In right apical lesions of some standing, even when the physical signs are slight, the right border of the absolute cardiac dullness may be found three-quarters to one inch or more to the right, or about the middle of the sternum. This Turban<sup>3</sup> considers "a typical and cardinal symptom" of tuberculosis of the right apex. Displacement of the heart to the right attracts our attention much more quickly than displacement to the left, on account of the difficulty of determining the exact boundary of the contracting lung and heart.

<sup>1</sup> Second Annual Report, Philadelphia, 1906, 239.

<sup>2</sup> Diagnosis and Treatment of Pulmonary Tuberculosis, 1908, 83.

<sup>3</sup> The Diagnosis of Tuberculosis of the Lungs, 1906, 81.

When extensive cavity formation has occurred on the right, when the right lung is the seat of fibrosis consecutive to pulmonary tuberculosis, or, as some affirm, to pleurisy, or a pneumothorax or a pleuritic effusion supervenes upon the left side, the heart may frequently be entirely upon the right side. Pulmonary tuberculosis is by far the most frequent cause of non-congenital dextrocardia, but this usually develops only when the left lung is slightly affected and is not bound down by pleuritic adhesions. It is, however, not common in pulmonary tuberculosis, but five instances being mentioned in 2344 cases at the Phipps Institute.<sup>4</sup> This dislocation may occur gradually, but in a few instances seems to take place suddenly, and the patient's attention is drawn in a short time to the fact that his heart is on the wrong side. Sudden transposition is probably due to the giving way of slight adhesions or to sudden changes of pressure in the pleural cavity: for instance, that produced by acute pneumothorax. Several years ago a patient of mine, with extensive cavity formation on the right side consulted me about his heart, which he said he had suddenly found on the right side. I had not seen him for some months, as he had been at work, and at the last examination I had noted no change in the position of the heart, although some must have been present. When I examined him I found the point of maximum impulse visible and palpable in the fourth interspace, on the right, just inside of the mid-clavicular line. There was a wide area of pulsation, and the dulness attributed to the heart was all to the right of the sternum and extended out as far as the anterior axillary line and above to the third rib. The patient continued at work, but suffered more and more from dyspnoea, which at last became extreme, and he was compelled to give up work two days before his death. At autopsy the pericardium was firmly bound down and extended on the right to about the anterior axillary line, above to the second intercostal space, and slightly to the left of the mid-line. The right lung, about one-third its normal size, was completely excavated. In another patient the dextrocardia was due to the same cause.

Young,<sup>5</sup> of Boston, has recently reported a case in which a gradual transposition of the heart occurred. Meyer,<sup>6</sup> of Hoboken, has had 3 cases of dextrocardia, all in fibroid phthisis, 2 of which occurred suddenly.

In an interesting case of valvular pneumothorax from the rupture of the wall of a cavity in the lower part of the left upper lobe the heart was a number of times gradually forced over on the right side, but it always returned when a needle was introduced and the air allowed to escape.

Marked displacement of the heart occurs much more frequently

<sup>4</sup> Loc. cit.

<sup>5</sup> Boston Med. and Surg. Jour., 1907, clvii, 791.

<sup>6</sup> Personal communication.

to the left than to the right, due, possibly, to the fact that the tension when the left lung contracts is exerted more directly upon the heart. For these reasons a very frequent displacement of the heart is upward and slightly outward. The heart, however, may be so greatly displaced to the left, following contraction of the left lung, or pneumothorax or pleuritic effusion on the right, that the apex may be beyond the left anterior axillary line or in the third intercostal space.

The heart is rarely displaced directly upward and more rarely directly downward. Mendl and Selig<sup>7</sup> have found the heart more perpendicularly placed.

**THE SIZE OF THE HEART.** The heart has been held by different authorities to be small, large, or normal in size in pulmonary tuberculosis.

*The Small Heart.* Since Laennec<sup>8</sup> first announced that the heart is small in pulmonary tuberculosis many famous authorities have argued for and against this belief. Beneke<sup>9</sup> is said by Blumenfeld to have been the first to prove by autopsy that the heart is small in pulmonary tuberculosis, and Brehmer<sup>10</sup> the first to hold congenital hypoplasia to be the cause of pulmonary tuberculosis. Hutchinson<sup>11</sup> believes that the heart is small and approaches the size that is normal at puberty, due, he suggests, to an arrested development similar to that which he holds takes place in regard to the shape of the chest. Many theories have been advanced to account for the smallness of the heart which undoubtedly exists in a number of patients who have died of pulmonary tuberculosis. It has been attributed to a poor appetite (Rokitansky<sup>12</sup>), impoverished nutrition (Potain<sup>13</sup>), cachexia (Louis,<sup>14</sup> etc.), atrophy or degeneration of the heart substance (Ratner<sup>15</sup>), lessened amount of blood and fewer erythrocytes (Stokes<sup>16</sup>), or to several of these factors.

Postmortem observations are not entirely satisfactory for the solution of this problem, for, as some affirm, antemortem changes in the size of the heart cannot always be detected at necropsy, but the musculature can be much more accurately measured. However,

<sup>7</sup> Prager med. Woch., 1907, xxxii, 529.

<sup>8</sup> De l'auscultation médiate, Paris, 1819, ii, 291.

<sup>9</sup> Quoted by Blumenfeld, Spec. Diet. u. Hyg. d. Lungen.- u. Kehlkopfschw., Berlin, 1897, 72.

<sup>10</sup> Die Aetiologie der chronische Lungenschw., etc., 1885, 143; and Die chronische Lungenschw., 1869, 57.

<sup>11</sup> Med. Record, 1906, 340.

<sup>12</sup> Manual of Pathological Anatomy, Swaine's translation for the Sydenham Society, 1854, i, 316.

<sup>13</sup> Quoted by Norris, loc. cit., Gas. hebd. de méd. et de chir., 1891, 441.

<sup>14</sup> Recherches anatomico-pathologique sur la phthisie, 1825, 54.

<sup>15</sup> Du cœur dans la tuberculose, Thèse, Paris, 1898 (quoted by Sequer, Le cœur des tub., Thèse, Paris, 1903, p. 9).

<sup>16</sup> Diseases of the Chest, Dublin, 1837, 414; Diseases of the Heart and Aorta, Phila., 1855, 546.

it may be, Reuter<sup>17</sup> (1884), in 261 autopsies (on patients with pulmonary tuberculosis), found a small heart in 29 per cent. of the men and in 56 per cent. of the women. Spatz<sup>18</sup> found a small heart in 327 autopsies with a tendency to hypertrophy of the left ventricle. Sequer,<sup>19</sup> in 270 autopsies, found the heart small in 24.5 per cent. of 200 men and in 50 per cent. of 70 women. This atrophy occurred more in young patients with rapidly fatal ulcerative processes and tuberculous enteritis. It was more pronounced than in carcinoma, due, he believed, to a smaller amount of blood and to less blood space. Norris<sup>20</sup> thinks that in uncomplicated pulmonary tuberculosis the heart is often subnormal in size, due to atrophy of its substance, and not to congenital hypoplasia.

More recently considerable work has been done to clear up this point, and the orthodiagraph and more exact methods of comparing the size of the heart to that of the body have been employed. Bouchard and Balthazard<sup>21</sup> with such methods have found that in men the heart at first is small but later is enlarged (hypertrophy and dilatation), while in women this is not so marked. Sciallero,<sup>22</sup> by use of the *x*-rays, decided that in the young and in those with recent lesions the heart is small and behind the sternum. During the past year Mendl and Selig<sup>23</sup> have stated that the heart is small in comparison to the body.

*The Large Heart.* If, as Krehl<sup>24</sup> believes, the same amount of blood is driven through the lungs until the pulmonary vessels are reduced three-quarters in volume, it is readily seen that the remaining vessels must increase in size or dilate, or pressure in the pulmonary artery will increase, the right ventricle hypertrophy, and the second sound at the pulmonic area become accentuated. The factors occurring in pulmonary tuberculosis and leading to hypertrophy are pleural adhesions, emphysema, a reduced capillary area, whether due to pulmonary fibrosis or sclerosis, or possibly to marked infiltration and complications, such as nephritis, arteriosclerosis, etc. Few observations indicating enlargement of the heart in pulmonary tuberculosis have been made until recently, and even some of these authorities have attributed the hypertrophy in many cases to alcohol (Bauer and Bollinger,<sup>25</sup> Reuter<sup>26</sup>) or nephritis (Sequer,<sup>27</sup> Norris<sup>28</sup>). Hypertrophy occurs more frequently in men (due some say to alcohol), more often in the fibrous form, and accord-

<sup>17</sup> Ueber die Grössverhältnisse des Herzens bei Lungentuberkulose, Dissert. München, 1884.

<sup>18</sup> Deut. Arch. f. klin. Med., 1882, xxx, 138.

<sup>19</sup> Le cœur des tuberculeux, Thèse, Paris, 1903.

<sup>20</sup> AMER. JOUR. MED. SCI., 1904, cxxviii, 649.

<sup>21</sup> Le cœur des tuberculeux, Rev. de la tub., 1903, x, 1.

<sup>22</sup> Semaine méd., 1902, xxii, 377.

<sup>23</sup> Clinical Pathology, translated by Hewlett, 1905.

<sup>24</sup> Quoted by Norris, loc. cit.

<sup>25</sup> Loc. cit.

<sup>26</sup> Loc. cit.

<sup>27</sup> Loc. cit.

<sup>28</sup> Loc. cit.

ing to Sequer<sup>29</sup> more often in older patients, who emaciate slowly. Renal tuberculosis has not been found to cause hypertrophy (Sequer,<sup>30</sup> Reuter<sup>31</sup>). In some recent experiments on rabbits by Hellin,<sup>32</sup> it was found that excision of one lung led to compensatory enlargement of the other and hypertrophy of the heart. The difference between these animals and patients with pulmonary tuberculosis, especially in an advanced form, lies in the fact that in the animals the musculature (general and cardiac) was normal, the volume of blood not reduced, and there was no toxemia present. Whether these factors are sufficient to explain why hypertrophy is not more frequent, I shall have to leave open. Palhier,<sup>33</sup> indeed, believes that hypertrophy occurs only when pathological changes are found elsewhere in the body.

Norris<sup>34</sup> states that enlargement of the heart (hypertrophy and dilatation) is said to occur five times more frequently at postmortem (about 12 per cent.) than clinically (as determined by percussion and auscultation). Reuter<sup>35</sup> found an enlarged heart in 40 per cent. of the men and in 20 per cent. of the women; Hirsch,<sup>36</sup> in 44 per cent.; Lebert<sup>37</sup> in 21 per cent. of those with chronic and 13 per cent. of those with acute disease; and Sequer<sup>38</sup> in 50 per cent. of the men and 16 per cent. of the women who came to autopsy. In 200 autopsies at the Phipps Institute<sup>39</sup> hypertrophy was present 13 times, 6 times of the left ventricle, 2 of the right, and 5 of both. These statistics are based upon autopsy findings, and most of the authorities state that the hypertrophy is found chiefly in the right ventricle.

The clinical statistics bearing upon the size of the heart are meagre. From the elaborate table of circulatory disturbances in pulmonary tuberculosis published by the Phipps Institute<sup>40</sup> no idea of the size of the heart from clinical observations can be obtained. At the Adirondack Cottage Sanitarium the heart was normal in size in the vast majority of 1289 patients, and only in 8, 6 of whom had valvular disease, was hypertrophy noted.

The diagnosis of enlargement of the heart in far advanced stages, when fibrosis and contraction or emphysema are often pronounced, must, if made, rest upon the accentuation of the pulmonic second sound and increased epigastric pulsation or, indeed, the use of the *x*-rays. If the general nourishment be maintained at par or be increasing, if the general blood pressure remain normal, and if there be rapid heart action and an accentuation of the second pulmonic

<sup>29</sup> Loc. cit.

<sup>30</sup> Loc. cit.

<sup>31</sup> Loc. cit.

<sup>32</sup> Arch. exper. f. Phar., 1906, lv, 21.

<sup>33</sup> Contribution a l'étude anatomo-pathologique du cœur dans la phthisie chronique, Thèse, Paris, 1890 (quoted by Sequer, loc. cit.).

<sup>34</sup> Loc. cit.

<sup>35</sup> Loc. cit.

<sup>36</sup> Deut. Arch. f. klin. Med., 1899, lxxiv, 615.

<sup>37</sup> Berl. klin. Woch., 1867, 233.

<sup>38</sup> Le cœur des tuberculeux, Thèse, Paris, 1903.

<sup>39</sup> Third Annual Report, Phila., 1907, p. 163.

<sup>40</sup> Loc. cit.

sound, cardiac hypertrophy is in all probability taking place, even though absent on clinical examination (Emerson<sup>41</sup>). Reuter<sup>42</sup> believes that a "bad" heart renders an individual more susceptible to tuberculosis and states that Bollinger<sup>43</sup> called his attention to the fact that cattle are more susceptible to tuberculosis than horses in which the heart is relatively almost twice as large.

Woods Hutchinson<sup>44</sup> has shown that all classes of animals with a relatively small heart in proportion to their body weight are very susceptible to tuberculosis, while others of the same general, with proportionately larger hearts are almost immune. This holds true he states, for birds or mammals, herbivora, carnivora, or omnivora.

*The Heart Normal in Size.* Variations from the normal are much more apt to occur in later than in the earlier stage of the disease, and in most patients in the earlier stage of the disease the heart is normal in size. In the majority of patients Sokolowsky<sup>45</sup> believes the heart is normal in size, and my observations on patients in the earlier stages of the disease lead me to the same conclusion. Later in the disease the heart may remain normal, as Sequer<sup>46</sup> found at autopsy in 25 per cent. of men and 33.3 per cent. of women, Harris and Beale<sup>47</sup> in 64 per cent., and Reuter<sup>48</sup> in 30.7 per cent. of men and 23.2 per cent. of women. Sciallero<sup>49</sup> found, by the use of the x-rays, the size of the heart to be normal in older patients and in those with chronic and benign lesions.

It may be stated then that congenital hypoplasia is infrequent, that the heart in the majority of early cases is normal in size, and that with progression of the pulmonary lesion the heart may, in the order of frequency, atrophy, hypertrophy, or remain normal in size.

**DILATATION.** Dilatation of the heart occurs far less frequently than would be supposed, and, as is to be expected, late in the disease. Laennec,<sup>50</sup> Louis,<sup>51</sup> and others noted it as exceptional. It has been found more in acute types of the disease (Brun-Bordeaux<sup>52</sup>), especially when they occur in patients with chronic fibroid changes. In acute miliary tuberculosis of the lungs dilatation and hypertrophy of the right ventricle are not rare, and are essentially a mechanical result, due to the impeded pulmonary circulation. Sequer,<sup>53</sup> in 271 autopsies, found it present 21 times in patients with fibroid, 7 times in patients with ulcerative forms. At the Phipps Institute<sup>54</sup> dilatation of the right heart was noted clinically in 9 per cent. of 1491 patients, usually in a far advanced stage, and at autopsy in

<sup>41</sup> Personal communication.

<sup>42</sup> Quoted by Reuter, loc. cit.

<sup>43</sup> Klinik der Brustkrankheiten, 1906, 237, 397.

<sup>44</sup> Treatment of Consumption, 1895, 201.

<sup>45</sup> De l'auscultation médiate, 1819, ii.

<sup>46</sup> Recherches anatomico-pathologique sur la phtisie, Paris, 1825, 51.

<sup>47</sup> Contribution à l'étude des maladies du cœur droit dans la phtisie, Thèse, Paris, 1877 (quoted by Sequer, loc. cit.).

<sup>48</sup> Loc. cit.

<sup>49</sup> Third Annual Report, 1907, pp. 39, 163.

<sup>42</sup> Loc. cit.

<sup>43</sup> Loc. cit.

<sup>44</sup> Loc. cit.

<sup>45</sup> Loc. cit.

24 per cent. of 200 cases. Jaccoud<sup>55</sup> has frequently found dilatation. According to Norris,<sup>56</sup> it occurs clinically in 32 per cent., at autopsy in 21 per cent. of patients with pulmonary tuberculosis. He explains this difference by the fact that retraction or consolidation of the lung increases the area of heart dulness, that most of the very ill patients remain in bed and so relieve the heart, and further, that extreme emaciation, usually present at death, affects the heart also.

In fibroid phthisis, in which emphysema, pulmonary sclerosis, and pleural adhesions tend to diminish the field of hematosis and the respiratory area, the tension is increased in the pulmonary artery, dilatation of the right side of the heart occurs, and tricuspid insufficiency, venous stasis, oedema, and asystole all hasten the end, which occurs more from the condition of the heart than from that of the lungs. The reserve force is said to be lessened in pulmonary tuberculosis. Dilatation of the right side (both auricle and ventricle) is often accompanied by hypertrophy of the right ventricle, which Jaccoud believes is favorable.

The area of cardiac dulness was rarely changed in 1289 patients at the Adirondack Cottage Sanitarium unless some valvular disease was present. In fact, all murmurs were classed as functional when there was no change in the area of cardiac dulness and when no definite cardiac symptoms were present. In 55 patients absolute cardiac dulness was noted as absent. In 2 patients the area of relative cardiac dulness was increased to the left, in 1 the disease was on the left, in 1 on the right, but neither patient was considered to have had valvular disease.

Patton<sup>57</sup> states that in tuberculous toxemia a dilatation of the conus arteriosus may occur, the apex impulse may be weak and diffuse, a systolic bruit may be present over the pulmonary area, and the pulse may be weak and empty.

**AUSCULTATORY PHENOMENA.**—Careful auscultation of the heart reveals, in a certain proportion of patients with pulmonary tuberculosis, some deviation from normal. A study in regard to the heart of 1289 patients at the Adirondack Cottage Sanitarium showed that 65 per cent. presented some slight variation from normal in their history or physical examination, while for the various stages the figures were: incipient, 63.5 per cent.; moderately advanced, 64 per cent.; and far advanced 79 per cent. (only 24 cases).

Much stress has been laid by Flick<sup>58</sup> and his fellow-workers upon the frequency with which the second pulmonic sound is accentuated. In 1491 patients, chiefly in far advanced stages, it was found accentuated in 664 (45 per cent.), and in 26 per cent. the aortic second

<sup>55</sup> *Traité de pathologie interne*, 1871, ii, 93.

<sup>56</sup> *Second Annual Report*, Phipps Inst., 1906, 243.

<sup>57</sup> *Colo. Med. Jour.*, 1904, x, 261.

<sup>58</sup> *Third Annual Report*, Phipps Inst., 1907, 39.

sound was accentuated. In 967 (75 per cent.) of our 1289 patients the heart sounds were found of normal relative intensity (the second pulmonic slightly louder than the second aortic sound). In the remainder the second pulmonic sound was accentuated 69 times (in 5 per cent. of the whole), and the second aortic was louder than the second pulmonic sound in 65 (5 per cent. of the whole). A weakened first sound is rather frequent in well-advanced stages, and is often more pronounced during acute attacks.

Functional murmurs were present in 81 patients (6 per cent.) of 1289 at the Adirondack Cottage Sanitarium, and in 17 patients (2.6 per cent.) of 639 at the Phipps Institute,<sup>59</sup> but the latter were in much more advanced stages when such murmurs would seem more likely to occur. At the Phipps Institute<sup>60</sup> the murmurs were heard 10 times at the base (7 over the pulmonic area) and 7 times at the apex. At the Adirondack Cottage Sanitarium the murmurs were about equally divided between the apex and the base (37 and 38), but at the base the murmur was much more frequent in the pulmonic area (including those in which the murmur was heard with greatest intensity over the pulmonic area, 35 times, and over the aortic area only 3 times, all systolic in time). In 6 patients the murmur was equally intense at both mitral and pulmonic areas. The murmur was widely transmitted, due, no doubt, in some cases to consolidation, in 10 of the apical and 6 of the basal (pulmonic) murmurs. At the apex the murmur was systolic in time in 33, diastolic in 3, and both diastolic and systolic in 1. Over the pulmonic area the murmur was noted as "presystolic" once. In 6 instances the murmurs were stated to be cardiorespiratory, but many more undoubtedly belonged to this class. In 3 patients a pleuro-pericardial friction rub was noted; in 2 it was systolic in time (once over the mitral, once over the tricuspid area), and in 1 diastolic, over the pulmonic area. A systolic whiff due to compression of a cavity during systole is not very rare and murmurs may be produced in cavities by the systolic distention of a large vessel or of an aneurysm.

In one male patient, a clerk aged thirty-seven years, denying lues, using little alcohol, and doing clerical work, a continuous murmur almost musical in character, with a systolic intensification, was heard over a wide area on the right back, with its maximum intensity opposite the seventh vertebral spine and 3 cm. from it. It was loudest just before the end of the expiration and decreased during the first part of inspiration. The x-ray examination showed no especial increase of shadow, the heart was apparently normal, cyanosis was absent, and the pulse normal. A diagnosis was made of pressure upon the great vessels by a tuberculous gland. The

<sup>59</sup> Third Annual Report, 1907, 40.

<sup>60</sup> Loc. cit.



patient had a slight consolidation of the right upper lobe and has done well.

A systolic murmur in the subclavian artery, first described by Stokes, is not infrequent, but is probably due to compression of the artery, and consequently is not connected with the heart.

Reduplication of the heart sounds has been rarely noted at the Adirondack Cottage Sanitarium, occurring 14 times (1 per cent.) in 1289 patients. It occurred in connection with the second sound at the pulmonic area in 3 cases, with the second sound at the apex in 3, with the first in 1. In 2 the second sound at the base and in 1 the second sound at the apex and base was reduplicated. At the Phipps Institute<sup>61</sup> the first mitral sound was reduplicated in 4 per cent. (of 652 patients) and the pulmonic second sound in 2.5 per cent. (of 652 patients).

Irregularity in the heart action and the skip of a beat is infrequent in early stages (6 per cent. at the Adirondack Cottage Sanitarium), and apparently less common in late stages (4 per cent. in 635 patients at the Phipps Institute<sup>62</sup>).

The radial vessel wall was noted as palpable or thickened in 74 patients (5.7 per cent.), 17 of whom were over forty years and 9 over forty-five years of age. According to the stages it was found in the incipient 21 times (4 per cent., 2 over forty-five years of age), in the moderately advanced 50 times (6.6 per cent., 6 over forty-five years and 13 over forty years), and in the far advanced 3 times (12 per cent., 1 over forty years, 1 over forty-five years).

**THE PULSE.** The frequency and the tension of the pulse in pulmonary tuberculosis are early and often permanently changed. The size of the pulse, its fullness and regularity, bear less definite relation to the pulmonary disease than the frequency and tension, and often until the late stages are only slightly if at all abnormal. The radial pulse is said to be influenced by the position of the arm on the affected side when contraction of the apex has occurred. Foss<sup>63</sup> has found paradoxical pulse in 61 per cent. of 120 patients, while Sörgo<sup>64</sup> noted a weaker pulse on the affected side in 8 per cent. of 397 patients.

*Frequency.* The frequency of the pulse has been observed from antiquity, and until thermometry was introduced this was the most important single phenomenon in this disease. Since the use of the clinical thermometer has become so common, less attention has been paid to the study of the pulse. Unquestionably it is in pulmonary tuberculosis nearly as important as the temperature, and in many cases is far more accurate for prognosis. The pulmonary patient borders constantly upon the verge of excitement, and the visit of the physician or a call at his office will often increase the pulse

<sup>61</sup> Loc. cit.

<sup>62</sup> Fortschritte d. Med., 1904, xxii, 99.

<sup>63</sup> Loc. cit.

<sup>64</sup> Wien. klin. Woch., 1904, xvii, 1337.

twenty beats a minute. The best record is that taken at the patient's home by a nurse to whom he is accustomed. This instability of the pulse, so marked in many cases, has some connection with the decrease of blood pressure and a paresis of the vessels. Altitude increases somewhat the pulse rate, which may decrease in a short time or persist.

Increased frequency of the pulse is often a striking feature in pulmonary tuberculosis and is of great value in diagnosis, as it stands most often in direct relation to the activity and extent of the disease and strength of the patient. The majority of all patients have at first a slightly increased pulse rate (90 to 100), even when apyretic, and frequently when at rest in bed. The pulse rate and temperature may be independent, but more usually there is a rather close connection between the two, which some have tried to express by allowing ten beats for each degree of fever. An increase above this rate they think is due to cardiac weakness. Forced feeding may produce slight acceleration of the pulse for a time. In some cases the pulse shows increased rapidity for short periods, but this is rather unusual, as when it once becomes rapid it usually remains so for some time. Mental excitement, slight physical exercise, attacks of coughing, and a full meal have a strong tendency to increase the heart beats in early as well as in advanced cases. In the latter, however, the pulse tends to be constantly rapid, and, varying somewhat with the temperature, increases slightly every afternoon. The range is usually between 88 and 120. This tachycardia is seldom noticed by the patient. Often as the patient improves, and after the temperature has become normal, the pulse rate gradually decreases, but it may quickly fall to normal and remain so. Slight tachycardia may persist in healed pulmonary tuberculosis.

The cause of the increased frequency is still unsettled. It has been attributed to pressure upon the vagus by enlarged tracheo-bronchial lymph nodes, an explanation which certainly does not suffice in many cases. Brehmer<sup>66</sup> thought the underdevelopment of the heart and the overdevelopment of the lungs is an important factor. Another view is that it is due to the increased work thrown upon the heart by a narrowing of the lumen of the pulmonary vessels, or to a narrowing of the air passages, which Marie found diminished the number of respirations and accelerated the heart. A neuritis of the vagus, the fall in blood pressure, irritation of the sympathetic, increased irritability of the cardiac ganglia or muscle fibers, myocarditis, anemia, and dyspepsia, have all been suggested as factors. The most probable cause, especially in incipient stages, is a weakening of the cardiac muscle and its nervous control, due to the tuberculous toxin, but this hardly explains the persistent tachycardia in

<sup>66</sup> Die chron. Lungenschw., 1869, 57.

some healed patients. Valvular disease of the heart in pulmonary tuberculosis exerts little influence upon the pulse rate.

*Blood Pressure.* The blood pressure in many cases of pulmonary tuberculosis is lowered from the very outset and some have held that hypotension is present in the predisposed. A much greater variation between the blood pressure in a reclining and in an upright position exists in pulmonary tuberculosis than in health (Emerson<sup>66</sup>). Potain believes that this hypotension can be used to differentiate a true chlorosis from the secondary anemia of tuberculosis, but a study of our cases by A. F. Miller does not uphold this statement. The hypotension is held by many to be due to the tuberculin, which, in large doses, undoubtedly lowers tension (Teissier<sup>67</sup>). Small therapeutic doses do not exert this effect. As the disease advances and pronounced constitutional symptoms occur, the blood pressure becomes less and less, and 90 mm. Hg. (Riva-Rocci manometer, with a nine inch cuff) is not uncommon. When the pulmonary tuberculosis is complicated with emphysema, nephritis, arteriosclerosis, diabetes (Teissier), or cardiac hypertrophy, the blood pressure may be raised. Naumann<sup>68</sup> thinks that most hemoptysis occurs in patients in the early stages with transitory high pressure, but he used Gaertner's tonometer, and assumed a rather low pressure as normal.

*PALPITATION.* In the 1289 patients there was a history of palpitation at some time in 271 (21 per cent.), but it is a rare thing for patients in early stages to complain of this symptom. It is said to be more frequent at puberty and at the menopause, sometimes to precede hemoptysis and to accompany dyspepsia. Considering the neurosis present in many patients palpitation is not as frequent as would be expected.

## THE HEART DURING THE EARLY PERIOD OF CONVALESCENCE FROM ACUTE INFECTIOUS DISEASE.<sup>1</sup>

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THE condition of the heart, together with its proper management in the early period of convalescence following acute infectious disease, is without doubt a subject of very great importance to every practitioner of medicine. Nor has the importance of this subject been ignored. In every special treatise on heart disease and in every

<sup>66</sup> Loc. cit.

<sup>67</sup> Des lésions de l'endocarde chez les tuberculeux, Paris, 1894, 103.

<sup>68</sup> Zeit. f. Tub., 1903, v, 118.

<sup>1</sup> Read at a meeting of the American Climatological Association, Boston, June 9, 1908.

book on the practice of medicine some reference is made to it. I am obliged to remark, however, that frequently what is written or stated is insufficient, by reason of the small amount of space that is allotted to its consideration, or because the rules for our guidance which are laid down are too general, and their lack of specific directions in given instances make them relatively of little value. And yet, that the medical mind is certainly alive to the necessity of greater attention and care in behalf of convalescents, is evident, as shown by an appeal made occasionally for funds to build a hospital for them, or insistence through letters to medical periodicals speaking of the dearth and of the need of such institutions. Despite this, preventive medicine and the rules which should govern us intelligently, so as to ward off, or protect from, acute infectious diseases, have received far more thought and work, it seems to me, than the care and treatment of those who leave ill beds where such diseases have previously prevailed.

I would not be understood as in any sense deprecating the well-deserved labor given to the former by men of the broadest mind and most intelligent grasp. All I would do is to contend forcibly for the judicious help and guidance of those who deserve, in my judgment, equal study and equal thought. It is perhaps Utopian—certainly in our life and time—to hope to abolish entirely acute infectious disease. It is not Utopian, once the disease has occurred and been battled with successfully, during the acute period, to contend daily and continually for a sufficient length of time against its normal or complicating sequels.

In this connection I take it that no organ of the body more frequently requires our wisest government than the heart. Upon prevention of cardiac dilatation depends mainly all future vigor and well-being in a very large number of instances. Not that we should ignore the other organs; not that we should not consider carefully the recuperation of the system in general; not that we should not pay strict attention to brain fag, to nerve exhaustion, to muscular debility, to powers of assimilation, to general nutrition. Granted all this, and yet the heart easily stands out primarily and essentially among all, in the great majority of instances. This is true, notably, in typhoid fever, in diphtheria, in influenza, in pneumonia, and in scarlet fever. It is equally true and even more so in acute articular rheumatism. In the latter disease, however, the frequent accompaniments of cardiac degeneration or cardiac dilatation are so apt to be more or less pronounced endocarditis, or pericarditis, that we have a problem which is somewhat unlike that connected with the other acute infectious diseases referred to.

In what follows, in view of limited time, I shall be obliged to omit many facts and details of very great interest, and confine myself as closely as possible to some salient cardiac features which are more or less common to the diseases mentioned. In all of them the heart

muscle and the nerves governing heart action are, as a rule, affected organically, if the disease be at all severe and if it lasts its usual period. By reason of the divers toxic elements of each one of these diseases, more or less cloudy change and fatty degeneration, as well of heart muscle as of nerve fibre, may be found. Numerous small lymphoid cells are often shown in the interstices of the muscle fascicles. The separate muscle cells are swollen, and often the nuclei have disappeared. The muscle cell shows granular or fatty degeneration, and the striæ are less well marked. The muscular fibers are sometimes ruptured. The degeneration may be general throughout the heart, or limited and more pronounced in certain areas, and the rest of the heart be comparatively intact so far as is observed microscopically. Sometimes and at a late period of the acute stage of disease, the heart muscle has become hyaline, or even fibrous in certain portions. Fatty infiltration of the cardiac nerves and cloudiness of nerve sheath and irregularity of the cylinder axes are not infrequently noticed at autopsies. The heart is flaccid—the walls thin many times—or there may be occasional hypertrophic dilatation. The color varies from the sere and yellow leaf hue to a reddish brown color. The heart in both instances is easily torn. Endocarditis and pericarditis are rare—at least of pronounced degree. There may be a slight endocarditis of the cardiac walls, which has not extended to the valves, or there may be a little beading of the free margin of the mitral valve which has not gone farther and may, and usually does, disappear with time. Cardiac thrombi are often found, especially in the right heart, which is distended. These thrombi may be soft, cruoric, gelatinous; frequently in diphtheria and pneumonia they are fibrinous in great part and formed probably some hours, or days, previous to death.

In making autopsies after acute infectious disease, it is essential not to confound pathological lesions due to other and preceding causes with those due to the infectious disease we are investigating. This is especially true of the lesions of a preëxisting myocarditis, subacute or chronic, which might be mistaken for those due to the immediately previous infectious disease, unless we are very careful and rigid in our examination and interpretation of what we find. And even when we are most painstaking, there are conditions at times, so far as the heart is concerned, almost on the border line, and we cannot say precisely what has occasioned them. In those instances, particularly, in which the postmortem findings have to do with scarlet fever which has been complicated during life with marked rheumatic manifestations, or those of suppurative arthritis, the evident lesions of endocarditis, simple or ulcerative, or pericarditis dry, serous, or suppurative, will surely indicate the complicating dyscrasia.

From these considerations it is shown that at times the pathological lesions of the heart are various, and nerves, muscle, vessels

are more or less affected, and in a more or less advanced degree of pathological change, due to a combination of causes. Hence our affirmations as to what is and what is not caused by the previous acute infectious disease must be made guardedly. It is, however, highly probable in a given instance, and when the acute infectious disease has been grave, or prolonged, that myocarditis relatively acute is thus occasioned, and not by some doubtful cause acting a length of time previously and little by little.

One of the most obscure and unsatisfactory findings up to date, is what relates to cardiac reports in autopsies following influenza. Frequently, if not always, we are in great doubt as to what is result of influenza and what is due to previous or complicating disease. Moreover, about the correct diagnosis of the influenza we are often in great doubt. The bacillus which is regarded as characteristic of the disease by some physicians is of doubtful value to others, and to them does not establish the identity of the disease. Many cases of so-called "la grippe" are not "la grippe" at all. They are simply cases of ordinary tonsillitis, pharyngitis, bronchitis, otitis.

In those instances of heart weakness, or sudden death following acute infectious disease, we frequently assume that the cardiac muscle is degenerated, or, indeed, at the autopsy we find the evidence of it to the eye and to the microscope. On the other hand, while we may find evident cardiac dilatation postmortem, there is present, properly speaking, no organic changes in the heart. Now then, while we attribute heart failure to degeneration of muscular or nerve fiber when it exists, what do we say in those cases in which both muscle and nerves reveal nothing abnormal? It seems to me we must at least admit ignorance on our part as to what is the real cause of cardiac weakness at times, since muscular or nervous degeneration would only explain cases when it exists.

The cardiac thrombi often contain the bacteria of the disease and are a distinct menace to life, not only by reason of their mechanical transport, but also because of the metastatic abscesses which they give rise to in different structures and organs.

Such changes, briefly, are what we find at autopsies in these diseases. It is fair to assume that during life, in minor degree at least, similar pathological conditions exist even after the acute stages of the disease are passed and the patient has entered into what may be fairly termed the early convalescent period. This period is considered to be that during which the temperature has returned to the normal, the pulse is approximately the health standard, the appetite returns, and increased strength and vitality become more evident. The patients begin to express the desire to get out of bed. A little later, and after being out of bed for a few hours each day, they wish to go out of the room, or down stairs, and later to go out of the house for a drive or walk. When is the proper time for permission to do these things, and upon what symptoms or signs

should our judgment be based, especially so far as the heart is concerned—the most important of all the organs in this determination, as a rule? From my own observation, study, experience, I would specially emphasize the importance of what follows, as a guide, in a measure, of sane conduct in a given case.

In typhoid fever, I do not believe, as a rule, it is wisdom for the patient to sit up in bed even for a short time, for several days—usually a week or ten days—after the temperature has reached the normal. I do not believe he should leave his bed until he has sat up in bed several times at least, and finally without causing any very considerable changes in his heart action and in his pulse. If sitting up in bed causes much increased rapidity of pulse, with irregularity and occasional intermittences, the indication is to go slowly and make the sitting up very little, or not at all, for a while. If combined with these indications from the pulse there is a soft blowing, systolic, mitral murmur at the heart covering the first sound and combined with, or not, accentuation of the pulmonic second sound; if, without any mitral murmur, there is notable weakening and lack of tone to the first sound; and if with, or without, murmur the heart action is feeble, rapid, irregular, and now and then intermittent, I should deem the patient safer flat on his back than even sitting up in bed.

What is stated as regards sitting up in bed is true again when the patient has been permitted to get out of bed, to walk into an adjoining room, or to go down stairs. We should expect, the first time a patient sits up in bed, or gets out of bed, increased rapidity of pulse and frequently a blowing systolic murmur indicative of mitral inadequacy. But in a day or two, or a few days at most, the pulse should be less rapid, and while the blowing murmur may be still present the heart action is more forcible and the pulse less depressible. Again, if we take the blood pressure with Janeway's sphygmomanometer, there ought to be relatively moderate difference between what is noticed while still in dorsal decubitus, or sitting upright in or out of bed. Otherwise, we wisely cry a halt to any exertion at all, physical or mental. If the temperature, instead of being normal, is subnormal—down to  $97^{\circ}$  to  $97.5^{\circ}$ —I object to the patient's leaving bed, as a rule. If, with lowered temperature, the urine is also of markedly low specific gravity (1000 to 1010), and if I know it was normal in health and had kept a good specific gravity during the acute period of the disease, and if its quantity is lessened, or not at all increased, I most strongly object to the patient's getting out of bed, or, at all events, walking from one room to another. Subnormal temperature, with urine of low specific gravity and lessened quantity, and perhaps slightly albuminous, adjoined to increased rapidity of heart action and pulse and lowered force of both (with or without a mitral murmur), and with or without notable irregularity or intermittence of both heart

and pulse, means inadequate heart strength. When instead of increased rapidity of pulse and heart, notable slowness of both occurs, I am even more solicitous and careful of my patient, and dread more the advent of sudden heart failure. I have seen this come on after very slight exertion in both conditions, and be ushered in with sudden faintness and great pallor; or, again, the lips and finger tips became notably blue and cold. With these signs the patient had marked dyspnoea and a sense of goneness. By means of immediate stimulation, such states are usually recovered from rapidly, with only the passing fright remaining to remind one still to be very careful and watchful for some time to come. Later, and when the patient had been out to walk or to drive, and apparently seemed fairly well and strong, suddenly such an attack as that just described would occur again, and frequently without any evident cause. Again, some slight overexertion would be the obvious accidental cause.

Following attacks of the sort described, I have examined the heart carefully. Sometimes I have been convinced by physical exploration, notably by percussion and palpation, that the heart was dilated and that this dilatation was seemingly acute in nature. Again, while I believe such dilatation was present, it was difficult, even almost impossible, to demonstrate it. Behind this dilatation, when present, we should see cardiac muscular fibres and cardiac nerves which are still suffering, as a rule, from structural disease—in the way of cure, but not yet recovered. Are these cases due to both systems affected—the muscular and the nervous—or may we separate them? Occasionally I have thought I could. When I have seen a patient get out of bed, go downstairs, or go out and drive or walk, and return to bed later and feel better and stronger for the exertion, and show it by higher specific gravity of urine, normal temperature, even slight increase of it ( $99^{\circ}$  to  $99.5^{\circ}$  F. under tongue), increased blood pressure, and stronger and more regular pulse, I have been convinced that the cardiac nervous system and not cardiac muscle, might be at fault functionally or organically. The soft blowing mitral systolic murmur may exist for many weeks.

Finally, and when the other cardiac signs and symptoms were practically normal during the convalescent period, I have come to the conclusion that the murmur was due not to mitral regurgitation through lack of closure of the orifice caused by want of cardiac power, but to improper or badly coördinated nervous control of the cardiac systole. I have been of this opinion, and it has been strengthened when the patient found that if he used his mental faculties except in very moderate degree, both his eyes and brain were sensibly fatigued.

Of course, to any one recovering from typhoid fever, particularly, who has fallen a victim to the disease when his previous life had been preëminently an intellectual one (lawyer, clergyman,



scientist, etc.), it is especially desirable during convalescence to avoid or limit continuous mental effort. The powers of the mind come back slowly and, in my observation among the last, and I do not believe that the heart itself will often work absolutely well unless the cerebrum be also healthy structurally and functionally.

Is there any period of duration as to the possibility of fainting attacks during convalescence; as to the development of more or less cardiac inadequacy due to dilatation and caused immediately by muscular or nervous cardiac changes? In general terms there is not. It may last weeks, months, years. Such cases must be managed with the greatest care, watchfulness, knowledge, patience. Time alone, with proper hygienic conditions of pure air, pure food, proper rest, recreation, and many hours of sleep in the twenty-four, will bring the patient out as well as ever. Drugs may be used beneficially in proper amounts during the acute attacks. Of these none is so valuable as strophanthus, by the mouth or hypodermically, and followed immediately with the best brandy, whiskey, or ammonia. Subsequently, strychnine is useful in certain cases, coca in others, and digitalis also in a few instances, in small or moderate doses—especially the infusion made from fresh English leaves.

Personally, I have never tried the Nauheim treatment, natural or artificial, in the early convalescence from acute infectious disease. It has, however, been vaunted, by one physician at least, even in the acute stage of typhoid fever, and later in a convalescent patient from this disease with an extremely weak heart. A modified artificial Nauheim treatment, called the siphon method by Albert Abrams,<sup>2</sup> has demonstrated its favorable action by giving the pulse increased strength in such a patient. I am very glad to report, also, that Dr. Philip King Brown,<sup>3</sup> of San Francisco, has made use of the Nauheim bath treatment in several cases of pneumonia and typhoid fever in their acute stages, and speaks favorably of the results obtained, especially in pneumonia, as compared with those effected by drug stimulation. The average blood pressure was notably "higher and better sustained on the days that baths were given than on the days that drugs were given." It would be fair, therefore, to assume from this that we should obtain as satisfactory and even better results from the use of the Nauheim baths in the early convalescent period; but of this I have no experience, nor can I record that of others. It is for the future to decide.

In the later convalescent period of certain cases of influenza and typhoid fever, particularly when the heart remains weak and slightly dilated, I am confident that the Nauheim treatment, wisely given by experts, is often of unquestionable and great value.

In a suggestive and eminently practical paper, Dr. W. Parker

<sup>2</sup> Medical News, March 16, 1901.

<sup>3</sup> American Medicine, 1906, pp. 325-331.

Wooster<sup>4</sup> directs attention lately to the great value of affusions and other methods of using hydrotherapy in the convalescent period from *any* disease, "when death seems imminent from heart failure and when free stimulation with drugs had been made." More or less ineffectually affusions increase arterial tension and restore resistance in vessels when the heart requires them urgently.

In instances of sudden heart failure occurring during the early convalescence of acute infectious disease, suprarenalin or adrenalin by the mouth in tablet triturates, each containing  $\frac{1}{16}$  grain, or preferably in hypodermic solution of 1 to 1000, is unquestionably very useful, as has been frequently observed. Personally, however, I have learned to place great reliance upon tincture of strophanthus by mouth and hypodermically, and I do not feel like abandoning it at present for the newer drug, until I am satisfied it is more advantageous under like circumstances: in view of the fact that strophanthus acts almost wholly as a very rapid and efficient heart stimulant, whereas adrenalin acts almost as much in contracting small peripheral bloodvessels and thus raising vascular tone as it does in giving power to the heart itself. This double action, it seems to me, might be prejudicial instead of beneficial in those cases in which there is no vasomotor paralysis and which do not require the heart to be stimulated by increased functional vascular power.

Finally, I cannot emphasize too strongly the major importance as a remedial agent of rest. This rest must be absolute in extreme cases and frequently prolonged many days and many weeks. After typhoid fever, pneumonia, diphtheria, influenza, scarlet fever, it is important, as already noted, but after an attack of acute articular rheumatism the infectious nature of which is now certain, although the special microbe causing it is not yet universally accepted, it is the *sine qua non* of prophylactic treatment and of that of the disease. And why? Simply because without it the numerous cardiac lesions will inevitably occur; these fill our hospitals and our dispensaries, and are usually hopeless, so far as cure is concerned, and frequently are most distressing cases. Among the results of acute articular rheumatism, neglectfully or foolishly treated, cardiac dilatation accompanying and caused by chronic myocarditis is by far the worst sequel. Of course, it may be, and frequently is, accompanied by and aggravated by chronic valvular disease, but it is the chronic myocarditis and not the valvular disease per se which makes the outlook to the patient and to the physician most deplorable. All this, many, many times, may be prevented in great part, if not entirely, by rest: rest for the body, as for the mind, rest absolute and continuous for days and for weeks. I am very glad to add that nowhere is this absolutely essential treatment insisted upon with more force and ability than

<sup>4</sup> New York Med. Rec., June 6, 1905, p. 942.

in a paper read before the American Medical Association in June, 1907, by Dr. S. Solis Cohen, of Philadelphia.

Great or even moderate mental strain should be avoided during several months at least; the same is true of severe, continued bodily exertion. Either one or the other may occasion cardiac dilatation little by little, or suddenly. In either case the condition is often irremediable and sets up heart disease which will last as long as life lasts, and usually gets continuously or intermittently worse, though it may be held stationary at times and for a while. To the neglected or careless and ignorant management of the early convalescent period following acute infectious disease is due, in my judgment, the larger proportion of chronic cardiac disorders of most distressing disabling, and finally fatal, character from which youth and adult life suffer.

The immediate risk to life is probably greater in the convalescent period of diphtheria than it is in the other acute infectious diseases, and more than one sad, deplorable event has occurred in my experience. Not always do deaths follow when there has been ignorance or negligence. Despite all judicious care and proper management, unfortunately, they occasionally occur, and, moreover, when practically, during days or weeks, there had been no warning note or previous threatening symptom. Sudden cardiac paralysis occurs and the end comes, rapid almost as the lightning stroke. Again, there may be a slow, gradual asthenia, which nothing seems to conquer, and which, in final analysis, and allied with other paralytic symptoms, seems to be evidence of extensive cardiac degeneration of muscle and nerves.

In scarlet fever, the complicating nephritis of the third or fourth week of the disease throws additional strain upon an already weakened heart, and thus dilatation, or hypertrophy with dilatation, is occasioned. Whenever to the nephritis of scarlet fever during the early convalescent period marked rheumatic manifestations are added, we should be fearful lest endocarditis or pericarditis should endanger the heart already weakened and dilated. To guard this heart effectually, we should make use of the ice bag or hot water bag to the precordial region and give salicin internally, in moderate or large doses.

In croupous pneumonia, as I have shown previously more than once, we should guard our patients especially against blood clotting, which is prone to occur—more so than in any other acute infectious disease with which I am familiar. This we may do effectually by means of carbonate of ammonium judiciously given, or by means of citric acid agreeably administered as lemonade. As to the poison of la grippe, I have no special counsel to give other than to state that I believe a moderate amount of quinine, or, better still, cinchona bark, in the form of the compound tincture, is valuable as a general tonic, and possibly has special value as a protection against cardiac

dilatation. Certain it is that we cannot be too careful in the management of the early period of convalescence following "la grippe." How often do we see or read of patients who have apparently recovered from the acute attack of the disease, are without fever, whose appetite and strength are partially recovered, but who have a sudden relapse? They go out of the house, expose themselves to the weather, return to their accustomed pursuits, and for a few days or weeks, seemingly, they improve continuously and, indeed, are almost well; sometimes without obvious cause, sometimes as the immediate consequence, apparently, of mental or bodily strain, they become re-infected with the poison of the disease and are soon weak and prostrate again, and more so than during the original attack. In these instances sudden death occasionally occurs. Now, whether it be the threatening and weakened condition of the patient from the renewed grippal attack which alarms us, or whether it be the sudden death thus occasioned which shocks us, we may be sure that it is the weakened, structurally altered heart, or profoundly disturbed, functionally deranged central organ, which is the principal agent or precursor of long, painful invalidism or sudden fatal termination.

The prognosis of a given case during the early convalescent period must depend very much upon the previous health of the patient, and especially upon the previous condition of his heart. If the patient be young and hitherto well, the prognosis is usually fairly good, even though the infectious disease has been of severe type—barring untoward accident or complication. On the other hand, if the patient be near or past middle life, we should be more anxious. This is true especially of pneumonia and influenza, and more than of typhoid fever and diphtheria, mainly because the two former diseases attack the middle-aged more frequently than the other two. But in any particular case we are specially anxious, either because, knowing the previous history, we believe it possible or probable that there has been already a preëxisting myocarditis before the attack of the infectious disease, or because we know positively this condition, with or without valvular disease of the heart, has preëxisted. Under these latter circumstances the prognosis is notably graver, and frequently, as we know, both in pneumonia and influenza, the patient dies rapidly or suddenly during the early convalescent period, and the death is undoubtedly caused directly by cardiac degeneration.

As to any special drugs other than those I have mentioned being useful to shorten the infectious disease or ward off irretrievable disaster, I know of none except what are usually termed tonics. Of these, iron in some form is occasionally useful when there is evident anemia during the early convalescent period after infectious disease, caused or not by it. Incidentally the iron may strengthen

the weakened heart to resist dilatation, if not already present, to lessen it possibly, or prevent its increase, if it has already developed.

Finally, I would insist that when we consider that apart from rheumatism, syphilis, alcoholism, continued bodily strain, with poor food and hygiene, cardiac dilatation, acute or slowly developed, is mainly occasioned by ignorant, injudicious, careless treatment of the early convalescent period following acute infectious disease, we must recognize the immense importance of my subject to every practitioner of medicine. Inasmuch as I believe cardiac dilatation is a preventable disease in these instances, its importance is only still greater.

NOTE.—Since writing my paper I am delighted to know that by the will of the late W. W. Smith, architect, of New York City, the bequest of nearly \$3,000,000 is made to St. Luke's Hospital Corporation, New York City. Mr. Smith stipulates that the money be applied "to the care and relief of needy convalescent patients recovering from acute diseases and surgical operations and from these and other causes requiring care and treatment not obtainable in their homes, and without regard to religious belief or sex." Noble man, noble gift!

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### NON-FATAL COMA IN THE COURSE OF DIABETES.<sup>1</sup>

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THE case of diabetes here reported was observed clinically for a period of nine months. The patient developed coma, from which she recovered, and four months later died in hemiplegia. Postmortem examination was made. The opportunity to follow such a sequence of events being comparatively uncommon, the report is thought to be of sufficient interest to add to the records now accumulating with regard to coma in diabetes as well as coma in general.

*Report of the Case up to the Development of the Coma (In Brief).* A woman, aged forty-eight years, was admitted to the City Hospital, February 27, 1907. Her complaint was nausea. Syphilis had been contracted, but when was doubtful. The patient was of feeble mentality; talkative. There was considerable thirst, large appetite, and other symptoms of diabetes, which seemed to have existed for about two years. There was a moderate degree of general arteriosclerosis. Chart I presents the urinary findings up to the time the coma developed.

<sup>1</sup> Read at a meeting of the Association of American Physicians, Washington, D. C., May 12 and 13, 1907.

CHART I.—COMA IN COURSE OF DIABETES. RECORD PRIOR TO COMA.

Date.	Amount in c.c.	Specific gravity.	Albumin.	Casts.	Reaction.	Sugar.		Acetone.	Diacetic acid.	Urea in grams.	Symptoms.	Weight in lbs.	Diet.
						Fermentation.	Amount in grams.						
Feb. 22	2800	1038	+	+	Acid.	2.5	70	+	0	16.8	Those common to diabetes of about three years' duration. In addition, patient is feeble mentally and has arteriosclerosis. Feb. 13 and Mar. 31, slight incontinence of urine.	—	Restricted. Consisting largely of beef-juice, eggs, and milk.
" 25	1860 +	1030	+	+	"	2.8	—	+	0	15.7		—	
" 27	2400	1037	+	+	"	3.5	54	+	0	14.7		—	
Mar. 5	2400	1037	+	+	"	3.5	74	+	0	19.2		101-5	
" 7	2203	1030	+	+	"	3.7	82	+	0	22.3		—	
" 10	2450	1027	+	+	"	2.3	56	+	0	21.7		—	
" 13	2650	1032	+	+	"	2.9	77	+	0	15.2		—	
" 19	1460 +	1028	+	+	"	2.6	—	+	0	10.6		102	
" 25	2550	1028	+	+	"	—	—	+	0	18.4		103.5	
Apr. 12	960 +	1030	+	+	Neut.	—	—	—	—	—		—	
" 28	2480	1025	+	+	"	—	—	—	—	22.32		—	

*Report of the Coma.* For the first two and one-half months after the patient was admitted a detail examination of the urine was recorded (Chart I). This was then discontinued until June 3, when the house physician reported that the patient had recently become irritable, had refused to save the urine, and had considerable diarrhoea, which had resisted ordinary remedies. For several days past (June 3) she had complained of weakness and muscular pain, especially in the back. She frequently fell asleep in her chair. There was some incontinence of urine and feces (diarrhoea) at these times. On the day previous (June 2) she had slept in her chair the greater part of the day, but would arouse as persons approached, and remain awake while they conversed with her. On June 4 the drowsiness markedly increased; she responded only when shaken, and then complained in a heavy manner of general pain, and quickly lapsed into her former conditions. There was incontinence of urine and feces. The breathing was audible, like that of one in deep sleep. It was never labored or irregular, that is, no dyspnoea (Kussmaul) was observed. June 5, the patient could not be aroused. Alkaline treatment was instituted on this date: Milk diet; bicarbonate of sodium, xxx grains (2 grams) by mouth every hour; saline enemas, one pint (500 c.c.) every six hours; hypodermoclysis (saline), one pint (500 c.c.) twice daily. If the urine remained acid to litmus or the patient's condition did not improve, bicarbonate of sodium was to be administered subcutaneously and intravenously. If an alkaline reaction of the urine appeared, the quantity of bicarbonate of sodium was to be reduced. Chart II presents the urinary findings during the coma.

It will be observed in this table that during the coma the specific gravity fell; the volume for twenty-four hours was about the same as that before the coma; the reaction was acid until June 8; the sugar was much reduced; acetone and diacetic acid were present in small quantity and  $\beta$ -oxybutyric acid was absent; ammonia was low; indican was not increased and there was a moderate amount of albumin and occasional casts. With the clearing of the coma the diacetic acid and acetone disappeared (in this order), the amount of sugar and the specific gravity increased. The urine remained acid to phenolphthalin, but on June 8 was alkaline to litmus. This, together with the lessening of the coma, contra-indicated an increase in the amount of alkali to be administered. About 2070 grains (150 grams) had been given in three days, in addition to saline enemas and hypodermoclysis. If an acidosis of any severity were present in this case, it is evident that the amount of alkaline administered was insufficient to counteract it. The alkalizing of the urine, however, indicated that sufficient alkali had been administered to overcome such acidosis as was present. The importance of this, as a diagnostic point, will be referred to again.

CHART II.—COMA IN COURSE OF DIABETES. PERIOD OF COMA

Date.	Amount in c.c.	Specific gravity.	Albumin.	Casts.	Acidity in terms 1/10 Nor. NaHO.	Reaction.	Sugar.			Acetone. Per cent.	Diacetic acid. Per cent.	$\beta$ -oxybutyric acid. Indican.	Total grams N. in 24 hours.	Ammon. per cent. of total N.	Total amt. ammon. N in grams in 24 hrs.	Symptoms.	Treatment.	Diet. Total fluids.
June 3 1500	1030	+	+	—	—	Acid	—	—	—	+	—	—	—	—	—	Onset of coma: irritability; weakness; muscular pain; sleep in chair every hour by mouth; most of day; arouses and saline enemias. Of every converses as persons are 6 hours; hypodermoclysis; refuses to give up, saline 500 c.c. b. d.; urine or obey orders; till urine is alkaline; in trav. and subcut. sod. bic. if condition is worse.	Plan for alkaline treatment: sod. bic., gr. xxx every hour by mouth, 23 enemias. Of every 6 hours (2 qts.); hypodermoclysis, saline (500 c.c.).	Milk and water 38 ounces.
" 4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	Developing coma: asleep most of the day; responds only when shaken, then lapses into former state; no Kussmaul respiration.	—	Milk and water 54 ounces.
" 5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	Coma established; cannot be aroused; incontinence of urine, feces; no every hour by mouth, 23 Kussmaul respiration at any time.	Alkaline treatment begun: sod. bic., gr. xxx every hour by mouth, 23 enemias. Of every 6 hours (2 qts.); hypodermoclysis, saline (500 c.c.).	Milk, 34 oz. Water, 110 oz.
" 6 1680	1030	+	+	—	—	Acid	—	—	—	+	+	—	—	—	—	Coma continues; somewhat less marked; incontinence urine; specimen obtained by catheter, (2 qts.).	Sod. bic., gr. xxx every hour by mouth, 23 enemias. Of every 6 hours (2 qts.).	Milk, 38 oz. Water, 236 oz.
" 7 1478	1028	+	+	—	—	Acid	—	1	14.78	0.00193	0.00048	0	0	—	—	Coma lessening; heavy but can be aroused; "sleeps" all day.	2070 gr. sod. bic. by mouth; 6 qts. saline enemias; 500 c.c. saline subcutaneously in 3 days.	Milk, 30 oz. Water, 42 oz.



" 8	1680	1022	+	—	Alk.	2.5	—	45.36	+	+	0	—	—	Coma clearing: sleeping lightly all day.	Sod. bic., gr. xxx by mouth, 3 doses (90 gr.); saline enemata, $\mathcal{O}$ every 6 hours (2 qts.).	Milk, 52 oz. Water, 40 oz.
" 9	1350	1009	+	+ 2.5 c.c.	Alk. lit. acid phen.	0.69	1	13.50	0.0116	0.2299	0	0.6	0.04	10.6	641	" Milk, 18 oz. Water, 66 oz.
" 10	1410	1009	+	+ 0.6 c.c.	Alk. lit. acid phen.	0.46	0.52	7.32	0.00348	0	0	0.5	0.66	8.3	470	" Milk, 62 oz. Water, 12 oz.
" 11	1920	1010	++	+ 3.0 c.c.	Alk. lit. acid phen.	0	0.68	13.05	0.00464	0	0	0.6	0.23	13.8	860	" Milk, 72 oz. Water, 2 oz.
" 12	1710	1014	+	+ 2.8 c.c.	Alk. lit. acid phen.	0.69	0.66	11.7	0	0	0	0.8	0.85	14.0	122	" Milk, 48 oz. Water, 20 oz.
" 13	1860	1009	+	+ 1.6 c.c.	Alk. lit. acid phen.	—	0.24	4.46	0	0	0	0.6	0.67	18.5	1.21	Sod. bic., gr. xxx by mouth, 3 doses (90 gr.); 2 eggs.
" 14	1833	1015	+	+ 1.8 c.c.	Alk. lit. acid phen.	1.8	1.86	32.9	0	0	0	0.16	0.9	14.5	2.3	" Milk, 86 oz. Water, 46 oz. 2 eggs.

+ = present; 0 = absent; — = examination not made.



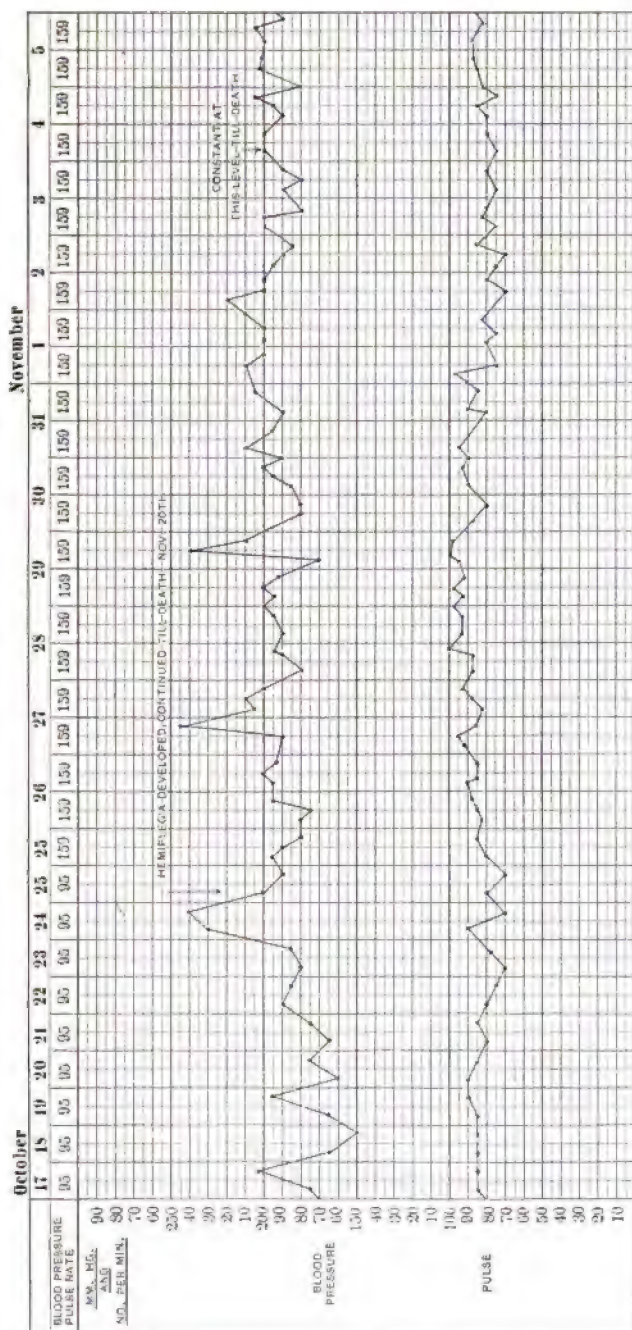


CHART IV.—Blood pressure for October and November; period of hemiplegia, just prior to death. Compare blood-pressure chart of this date with that of June, period of coma (Chart III).

On opening the thorax the left plural cavity is dry and free from adhesions, the right plural cavity is dry and contains a few adhesions over the apex and over the lower lobe in the axilla.

*Heart.* Mitral valves: Posterior valve cusp shrunk; anterior contains large, irregular patches, which are yellowish and have wavy raised edges. The aortic valves are wrinkled and slightly stiffened at their bases. The aortic above contains numerous gamboge-yellow raised patches. The coronaries are small, tortuous, and contain numerous deep, yellow, raised patches. The heart muscle on section is brownish with yellowish mottled areas; the muscle bundles are not distinct; in place there are small white areas.

*Left Lung.* The lung is small, its anterior portions crepitant, its posterior portions bluish, wet, œdematous. There are a few subpleural calcified tubercles, which are surrounded by black anthracotic areas. Upper lobe is crepitant, dry. The pleura at apex is negative. The lower lobe is firmer, wet, and exudes a small amount of frothy serum. The smaller bronchi are slightly reddened. *Right Lung.* The right lung is larger; the upper lobe contains a few puckered pleural thickenings, and on section it is reddish and exudes on pressure frothy serum. Some of the smaller bronchi exude purulent material, and the lobe contains scattered areas which are firm, but from which cut section sinks. The middle lobe is crepitant, emphysematous. The lower lobe is dark red, and contains scattered areas of consolidation, and exudes on pressure frothy serum. The smaller bronchi, especially those of the lower lobe, are bathed in mucopurulent material.

*Spleen.* Negative.

*Left Kidney.* Weight, 185 grams. The kidney is quite large, surrounded by a small amount of perinephric fat; it measures 13 x 7 x 4 cm. The capsule strips with some difficulty, leaving a finely, and in places roughly, granular surface. The lobulations are fairly well marked, and in places contain whitish puckered scars. On section the cortex has an average thickness of 10 mm.; it is yellowish and greasy; the Malpighian bodies not at all distinct. The medulla is reddish in color and the line of demarcation well preserved.

*Right Kidney.* Weight, 180 grams. Same as left.

*Duodenum.* Small, with well-marked rugæ. The papilla is prominent and exudes fluid bile on pressure. Common, cystic, and hepatic ducts free.

*Liver.* Weight, 1500 grams. Its surface is smooth, and contains mottled yellowish areas. On section it has a somewhat greasy surface. The centres of the lobules appear dark red in color. The periphery of the lobules is light yellow.

*Pancreas.* On removing the pancreas, which is rather small, the tail of the organ not reaching the hilum of the spleen, the weight is found to be 100 grams. The organ measures 17 cm. from head to tail. Its middle part is 5 cm. broad and 3 cm. thick. It is surrounded

by very little fat. On cut section, firm; the lobules are irregular in size, pinkish, and separated widely by bands which have a butter-like consistency. The pancreatic duct is apparently surrounded by a large amount of connective tissue. The splenic artery shows moderate atheroma. The pancreatic, common, and hepatic ducts and the gall-bladder are free from stones. Microscopic section shows interstitial and marked interacinar pancreatitis; sclerosis of and diminution in the number of islands; great destruction of pancreatic lobules, bringing islands into clumps.

*Brain.* The brain is small, there being apparently atrophy of both frontal lobes. The vessels at the base of the brain are small, tortuous, and filled with atheromatous plaques. On opening these vessels the lumen gaps and the walls are clotted. On section of the brain a small area of softening is found in the right internal capsule along the motor tract. This area is elongated, being about 5 mm. by 1 cm. It is entirely limited to the motor tract. There is also considerable fluid in both lateral ventricles. The brain substance around this area is very soft. In the right pons is also a small area of softening about 4 mm. in diameter, well localized. Along the motor tracts the spinal cord grossly shows no area of degeneration. The posterior spinal vessels, however, are thickened and tortuous.

ETIOLOGY OF THE COMA. 1. *Acidosis or Acid Intoxication.* At the annual meeting of the Association of American Physicians held in 1907 Dr. Folin<sup>2</sup> presented a review of the work done on acid intoxication, and Dr. Joslin,<sup>3</sup> at the same meeting, presented a similar paper on acidosis. From these two papers it appears that, though for the last fifty years much work has been done in Germany and in this country on the high ammonia content and organic acids in diabetes, there is as yet no clear knowledge of either the source of these acids or the part they play in the graver stages of this disease. The chemical features, however, of these conditions are now well established, and from the record here given it can be stated definitely that neither existed in this case. The ammonia remained unusually low throughout the coma, and the diacetic acid was present in small quantity only;  $\beta$ -oxybutyric acid did not appear at any time (Charts I and II). That it would be incorrect to assume the absence of acidosis upon this latter negative finding alone has been pointed out by several authors. Dr. Lusk, with Dr. Mendel, reported a case in which there was absolute intolerance for carbohydrates, and yet for three weeks no  $\beta$ -oxybutyric acid could be detected in the urine, and there was a maximum output of but 0.8 gram. of acetone daily. But this, together with the low ammonia, small total output of urine in twenty-four hours, and prompt alkalizing of the urine with small amounts of alkali (see discussion of treatment below), indicates the absence of acidosis or acid intoxication in this case.

<sup>2</sup> Trans. Assoc. Amer. Phys., 1907, xxii, 256.

<sup>3</sup> Ibid., p. 246.

2. *Uremia.* The urine showed nothing in regard to nephritis, which does not occur in many cases of diabetes. Albumin was present throughout. The great increase in the characteristic casts described by Kulz<sup>4</sup> did not occur at the time of the coma, though casts were at all times present. The most significant finding was the blood pressure (Charts III and IV). The blood pressure ran moderately low during the coma, but in the final attack, which was associated with hemiplegia, the pressure rose and remained uniformly high until death. Albuminuric retinitis showed definitely that nephritis was present. Autopsy showed a chronic diffuse parenchymatous nephritis, which, although indicated by the urine and retinitis, could not, from any clinical manifestation, be held accountable for the coma. Beyond the blood pressure changes and the absence of increase in albumin, we must consider that there were no clinical signs by which uremia as a cause of the coma could be included or excluded.

3. *Brain Softening.* This patient showed from the beginning mental weakness. There was a history of syphilis and evidences of general arteriosclerosis. This evidence was in hand at the time of the onset of the coma. Cases in literature are not lacking<sup>5</sup> to show the frequent association between diabetes and encephalomalacia. Four weeks before death hemiplegia developed, and definite evidence of this condition was found postmortem. At the time of coma, however, we had not these facts, and the stupor was different in no way clinically from graver forms in diabetes. The mental weakness, the incontinence of urine and feces, together with mild diabetes and absence of signs of acid intoxication, were important facts pointing to the central nervous system. The subsequent hemiplegia was very significant. There is no explanation as to how coma, in such brain conditions, is produced.

4. *Disturbed Protein Metabolism.* Although nitrogen partition was made in this case, it seems inadvisable to attempt conclusions from one case. This portion of the record, therefore, is omitted.

**ALKALINE TREATMENT.** This, while of no value therapeutically in the present case, proved to be so diagnostically. It will be remembered that treatment, as recommended by Stadelmann and followed by Naunyn and Magnus Levy, required 100 grams of bicarbonate of sodium a day. As high as 80 grams have been injected intravenously, the reaction of the urine being the guide to the quantity to be administered. In the case here reported 150 grams by the mouth in three days was sufficient to alkalize the urine. This was in itself evidence of either the absence of acid formation or, if present, in quantity insufficient to account for such grave clinical manifestations as appeared.

<sup>4</sup> Domansky and Reimann, *Ztschr. f. Heilk.*, 1901, and Herrick, *AMER. JOUR. MED. SCI.*, 1900, vol. cxx.

<sup>5</sup> Frerich, Ogle, Dreyfus, etc., cited by Naunyn.

**CONCLUSIONS.** From the foregoing evidences the case seems to have been one of syphilitic arteriosclerosis (history of syphilis, presence of arterial thickening, arcus senilis, and aortic cardiac sclerosis), with involvement of the pancreas, kidney, and brain. The sclerotic changes in the pancreas (interacinar pancreatitis) led to the diabetes, those in the kidney (chronic parenchymatous nephritis) to the chronic nephritis (albuminuria, casts, and albuminuric retinitis), and those in the brain to the softening with hemiplegia, to the feeble mentality, and possibly to the coma.

At the bedside, when the coma appeared, the syphilitic history, the arteriosclerosis, the enfeebled mentality, the mild grade of diabetes, the absence of any increase in the diacetic acid, the non-appearance of  $\beta$ -oxybutyric acid, the low ammonia, the small quantity of alkali required to alkalize the urine, the absence of any increase in total quantity of urine in twenty-four hours, seemed to be clinical features differentiating this coma from the graver forms. The subsequent hemiplegia was very significant. The low blood pressure and absence of any increase in albumin and casts were suggestive, but not positive signs by which uremia could be excluded. The urinary findings and the small amount of alkali required to alkalize the urine seem in themselves important guides in diagnosis and safeguards against false conclusions with regard to the part played by the alkaline treatment.

The only coma in diabetes clinically defined is the dyspnoeic type, and the only coma chemically defined is that due to acidosis and acid intoxication. The diagnosis of these conditions, as a rule, offers no great difficulty. It is the atypical group or that due to complications which occurs more frequently and which presents the real diagnostic and prognostic problem to the clinician. The nephritis and brain condition are most important in the consideration of the coma, but in the absence of any clear knowledge of how coma is produced in uremia or brain softening, the mere statement of their presence is not sufficient to exclude other factors resulting from disturbed metabolism (proteid for example) which subsequent investigation may disclose.

The discussion of the case with nine months' clinical record, and, finally, the postmortem findings before one is very different from the problem offered the clinician at the bedside at the onset of the coma. At that time it was impossible to say that fatal coma was not developing. I believe two important findings at that time justified one in assuming that the coma was of mild type, namely, the character of the urine and the amount of alkali required to neutralize the urine. In forty-eight hours from the onset of the coma these features manifested themselves. While no explanation of the coma appears in the record, these clinical findings may prove to be features differentiating the comparatively common non-fatal coma in diabetes (due possibly to complication or some yet

unexplained metabolic disturbance) from the rapidly fatal coma in this disease.

The laboratory examinations were done in the Strecker Laboratory under Dr. Oertel and in the Cornell Clinical Laboratory under Dr. Hastings. I wish to thank Drs. Woodruff and Groeschel, house physicians, for their interest and care in preparing the records.

Dr. Joslin kindly reviewed the records with regard to the question of acidosis, or acid intoxication, and his opinion is expressed in the following letter:

"In my opinion the case . . . illustrates coma simulating the coma of acid intoxication, and yet certainly has absolutely no connection with that form. It is essential for physicians to remember this possibility, and not to treat all cases of coma in diabetes as if due to acid intoxication. The case is further valuable because so often in the past cases of coma in diabetes have been said to occur without proving the acidosis. This case was carefully studied, acidosis eliminated, and coma proved to be of another type.

"The case was evidently mild diabetes, because the carbohydrate balance was pretty certainly, from the records given, positive rather than negative. For example, the greatest quantity of sugar was 84 grams on February 27, and yet evidently considerable milk was used at that time, and the diet probably contained more than this amount of carbohydrates. Further, the case was evidently mild, because there was no diacetic acid in the urine during February, March, April, and only a very small quantity in June. Diacetic acid constitutes only about 10 per cent. of the total acidosis, and acetone constitutes only about 10 per cent. of the combined acetone and diacetic acid. Consequently we are absolutely certain that the acidosis was insignificant.

"For the above reasons it is not necessary to know more details of the urine during the coma, because the analyses before and after settle the severity of the case. There are a few additional factors which help to exclude the acidosis: First, the fact that the urine became alkaline on June 8, during the coma, while the patient was taking an insignificant quantity of alkali, *e. g.*, 2 grams hourly. Second, the total quantity of urine at no time exceeded 2000 c.c. No case of diabetic acidosis, to my knowledge, has been reported without Nature making an effort, by the passage of large quantities of liquid, to wash out acids from the body. Third, the increase in the percentage of ammonia was very slight, and the total quantity far too low to enable one to claim acidosis."



**THE PATHOLOGICAL CHANGES IN THE THYROID GLAND,  
AS RELATED TO THE VARYING SYMPTOMS IN  
GRAVES' DISEASE.**

BASED ON THE PATHOLOGICAL FINDINGS IN 294 CASES.<sup>1</sup>

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THE material for the following study was obtained from operations and autopsies on cases of Graves' disease (hyperthyroidism, exophthalmic goitre) in St. Mary's Hospital, Rochester, Minnesota, from March 3, 1898 to May 10, 1908. The material in 2 of the cases was obtained at autopsy on patients dying of hyperthyroidism without having been operated upon. These autopsies were made within two hours of the death of the patient. All of the other material consisted of glands removed by Dr. C. H. Mayo.<sup>2</sup> Thirty-five of the cases were operated upon prior to the reorganization of the laboratory, January 1, 1905. When this study was begun there was not sufficient data at hand from which to make a complete pathological analysis of these 35 cases. No report, however, has been previously made on their pathology, and I desire, therefore, to place them now on record as fully as the data will permit, although they will not be considered in estimating the percentages of the pathological groups of the cases studied in full detail.

This series consists of: (A) 11 cases in young females whose symptoms had existed without remission or abatement from two months to two years, and who at the time of examination presented all the classic symptoms of Graves' disease in a severe form. The pathological diagnosis on all of these cases was noted at the time as "typical exophthalmic goitre." (B) 9 cases in females whose symptoms had existed from one to eleven years, but all of whom were better at the time of examination than they had been at some previous period. In all of these cases the pathological report is either "typical exophthalmic goitre," or "exophthalmic goitre with colloid." (C) 14 cases in females whose symptoms had been present from three to thirty years, or from three months to one year following a previous long period of non-symptomatic goitre, and at no time had shown symptoms of more than moderate severity. The pathological report on these cases is "colloid adenoma."

<sup>1</sup> To avoid future confusion Professor James Ewing authorizes me to state that the 40 cases reported by him in the New York Medical Journal, 1906, lxxxiv, 1061, 1114, were exclusive of the cases in this series, although he had also studied sections from a number of my cases.

<sup>2</sup> This series does not include 13 cases operated on by Dr. C. H. Mayo in other hospitals, since no material from these cases was obtained in our laboratory.

With the reorganization of the laboratory, January 1, 1905, with an increased staff and increased facilities, it became possible to take care of the pathological material to better advantage. Since that time all specimens are brought immediately from the operating room to the laboratory, where they are examined fresh and then placed in fixatives, usually within ten minutes after they are removed from the patients. Blocks of tissue from each are fixed in 10 per cent. formalin, absolute alcohol, Zenker's fluid, and Flemming's chromosmic mixture. The remainder of the specimen is then photographed and preserved by Kaiserling's method.<sup>3</sup> Microscopic preparations are made of the fresh material frozen and stained with polychrome methylene-blue, by the author's method,<sup>4</sup> and also of the formalin-fixed material, frozen and stained with hematoxylin-eosin. From the examination of these two preparations the initial histological record is made on the history sheets. When the final study was begun, material from the various fixatives was sectioned by the paraffin method and stained with hematoxylin-eosin, Heidenhain's iron hematoxylin, and Mallory's methylene-blue-eosin. The histology of each case was then carefully reviewed from all the preparations at hand, and notes made according to a formula compiled from the reports of previous observers.<sup>5</sup> As may be supposed the detailed data from these studies are much too voluminous to report in any one paper, and it is only that portion of it which seems to be related to the clinical histories to which I wish now to call attention.

While this review was in progress every care was taken to exclude all knowledge of the clinical histories of the cases in order that there might be no clinical bias entering into the pathological estimate. As the work proceeded it was found that certain pathological pictures were frequently repeating themselves. When the examinations were completed these pictures were found to represent cases constituting four large groups, and there was little trouble in arranging the remainder of the cases so as to form connecting groups between the large and more striking ones. The following cases presented from the pathological standpoint will illustrate these groups with sufficient accuracy for the succeeding clinical comparisons:

**PATHOLOGICAL GROUP A.** Case No. 24,550 (Fig. 1).—This specimen is a gland, the removed portion of which weighs 30 grams fresh. Grossly it is hard and nodular. The cut surface is particularly dry and granular throughout. There is considerable increased vascu-

<sup>3</sup> Some of the gross specimens have been sent to other laboratories. This material was not on hand at the time of the present review. In these cases the detailed review of the gross anatomy was made from written descriptions and photographs of the fresh specimens.

<sup>4</sup> Jour. Amer. Med. Assoc., December 2, 1905.

<sup>5</sup> It is proper to state that as a preliminary study about 300 simple goitres were examined and, as occasion arose during the progress of the work on the Graves' goitres, the former were again reviewed and compared with the latter.

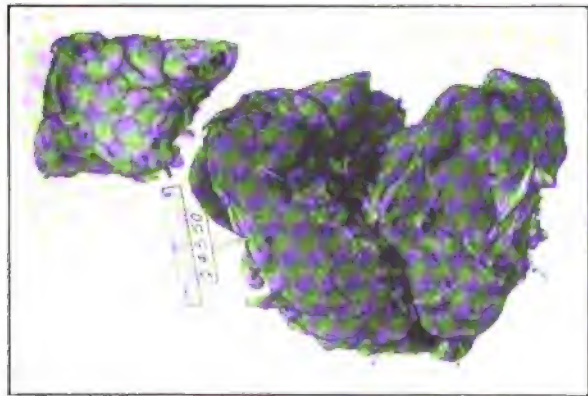


FIG. 1.—Photograph of the thyroid gland.  $\times \frac{1}{6}$ .

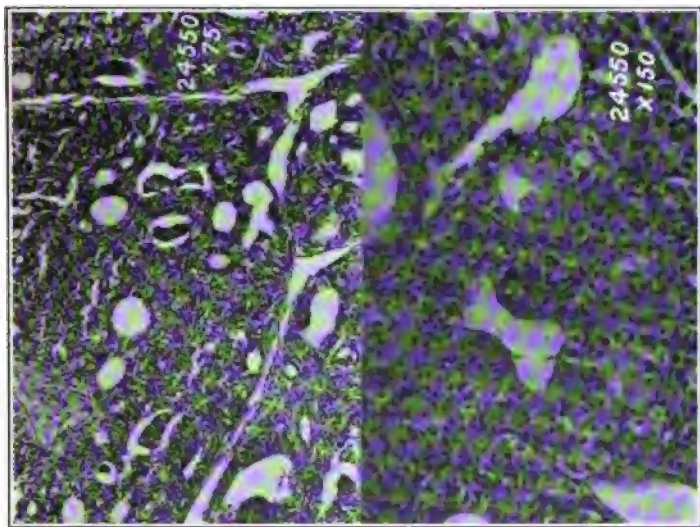


FIG. 2.—Photomicrographs.



FIG. 3.—Portrait before operation.

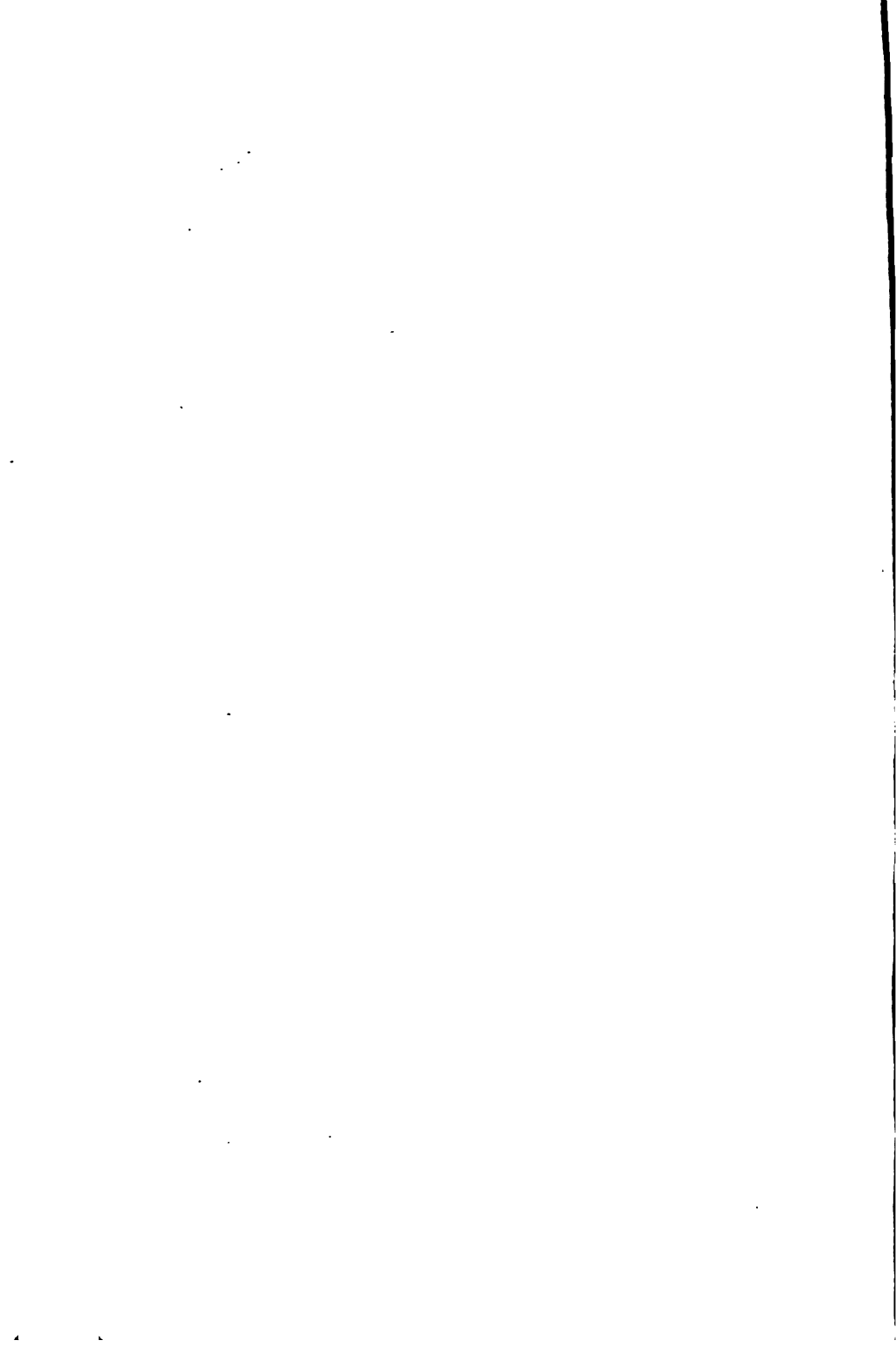




FIG. 4.—Photograph of the thyroid gland.  
×  $\frac{1}{2}$ .

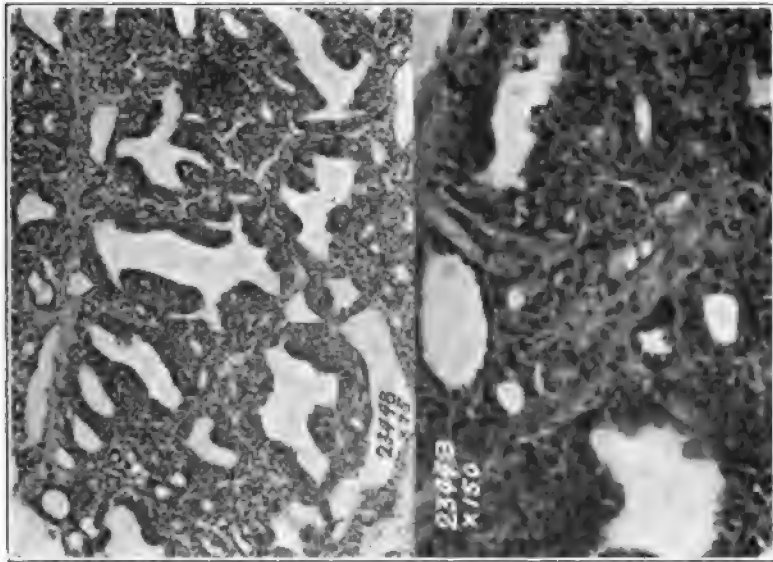


FIG. 5.—Photomicrographs.



FIG. 6.—Portrait before operation.





FIG. 7.—Photograph of the thyroid gland.  $\times \frac{1}{2}$ .

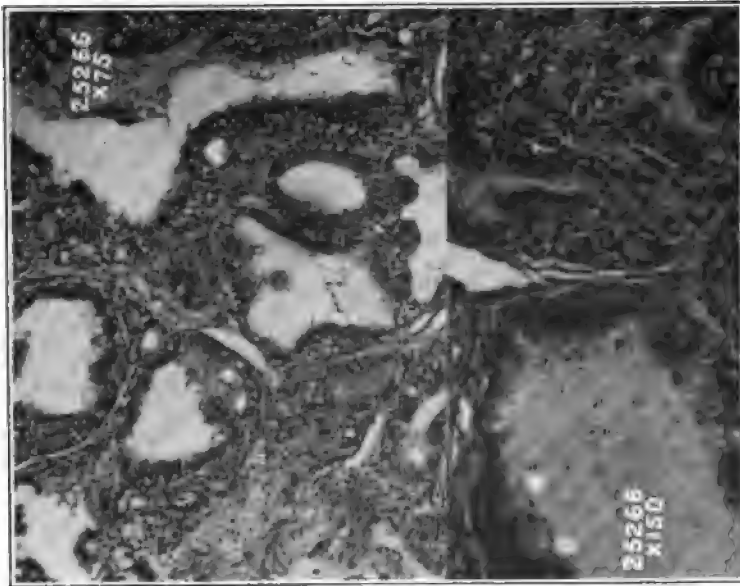


FIG. 8.—Photomicrographa.



FIG. 9.—Portrait before operation.





larity, the veins being swollen and thin walled. Microscopically (Fig. 2) the stroma bands are found considerably thickened and extensively infiltrated with leukocytes. The alveoli are from 0.06 to 0.2 mm. in diameter. There are very few papillary projections into the alveoli. The parenchyma cells are increased in number in certain alveoli, both in the single layers and by reduplication of the layers. The parenchyma cells are columnar, about 10 microns in diameter, have swollen nuclei, granular protoplasm, and show in many areas mitotic figures. There is apparently no exfoliation of the parenchyma cells. The secretion is small in amount and non-eosin staining. From the pathological standpoint the symptoms, if any, in such a case, should be those of very early, mild hyperthyroidism. The clinical history shows that the gland is from a female (Fig. 3), aged twenty years, who has had a slight symptomless enlargement of the thyroid for one year, and moderate Graves' symptoms for the last two months, that is, tachycardia, fine tremor, sweating, etc.

This case is representative of a very small group (Group A) of operated cases, there being but 3 patients (10 per cent.) in our entire list, although a number of other patients, of parallel clinical characteristics who have presented themselves for examination, would probably have yielded glands of similar pathology had they been operated upon.

The characteristics of this group may be stated as follows: 1. Small intra-alveolar parenchyma increase. Shown by: (a) Size of the gland; (b) increased number of cells in a single layer; (c) reduplication of layers. 2. Small amount of thin secretion. Shown by: (a) Dryness of the fresh section; (b) small amount of secretion in stained sections. This is non-eosin staining.

**PATHOLOGICAL GROUP B.** Case No. 23,448 (Fig. 4).—This is a 53-gram gland, hard and nodular externally, granular, with a slightly glairy cut surface. Histologically (Fig. 5) the sections show increased alveolar parenchyma, papillæ formation, and a large amount of non-staining secretion. Clinically (Fig. 6) the patient is a female, aged thirty-six years, who, after three years progressive Graves' disease, now shows severe symptoms, that is, nervousness, tachycardia, tremor, some diarrhoea and vomiting, and exophthalmos.

Case No. 25,266 (Fig. 7).—This is a 60-gram gland of the same character grossly as the preceding. Histologically (Fig. 8) there is a large amount of intra-alveolar parenchyma increase, papillæ formation, and a large amount of thin secretion. Clinically (Fig. 9) the patient is a woman, aged twenty-eight years, with a history of two years of Graves' disease, and at present severe symptoms, that is, tachycardia, nervousness, tremor, profuse sweating, some diarrhoea and vomiting, and exophthalmos.

Case No. 18,339 (Fig. 10).—This gland weighs 60 grams fresh, is hard and rigid, with a nodular outer surface. The veins are swollen, varicosed, and thin-walled. Histologically (Fig. 11) the section shows a picture almost parallel with that of the previous case, except that the alveoli here are larger and the papillary projections in them are numerous, while there is a large amount of thin, non-eosin staining secretion. Pathologically this case should be in the acute stage and severe in type. Clinically (Fig. 12) the patient is found to be a female, aged nineteen years, with Graves' symptoms for one year, and now of severe type, that is, nervousness, tremor, weakness, exophthalmos, and pulse 150.

Case No. 23,095 (Fig. 13). This is a 95-gram gland, hard and nodular, and dry and granular on its fresh-cut surface. The large, irregular alveoli (Fig. 14) are lined with swollen parenchyma cells which have not begun to exfoliate. The secretion is fairly large in amount, thin, and feebly staining. A severe first period is indicated pathologically. Clinically (Fig. 15) the patient is a woman, aged twenty-five years, who, for two months, has had a progressive chain of symptoms of hyperthyroidism, that is, nervousness, tremor, palpitation, tachycardia, exophthalmos, diarrhoea, and vomiting, and now would be considered a case of very severe grade.

Case No. 23,099 (Fig. 16).—This is a 120-gram gland, hard and nodular, with a granular, glairy, cut surface, and swollen tortuous veins. Histologically (Fig. 17) there are large alveoli with great intra-alveolar parenchyma increase, papillæ formation, and a large amount of thin, non-staining secretion. Clinically (Fig. 18) the patient is a female, aged thirty-six years, who has had progressive symptoms of Graves' disease for three years. They are now of a very severe type, that is, tremor, palpitation, tachycardia, diarrhoea and vomiting; exophthalmos for one year and a half.

Case No. 21,328 (Fig. 19).—This is a very large gland, weighing 223 grams fresh. It feels hard, has a nodular outer surface, and a glairy, cut surface. The veins are swollen and tortuous; the walls of the large vessels are thin, and there are many small hemorrhages with marked hyperemia throughout the gland. The alveoli, papillary projections, parenchyma cells, etc., are parallel to those in the previous cases as will be seen (Fig. 20). Pathologically this should be a severe acute case. Clinically (Fig. 21) the patient is a male, aged thirty-seven years, who has presented a set of symptoms of Graves' disease of gradually increasing severity for six years, and who is now in an extremely critical condition. There has been no remission of symptoms at any time in this case. His history shows he has lost forty pounds in weight in the last six months previous to operation.

These 6 cases illustrate quite fully pathological Group B. This is the largest group in the series, containing 117 cases, or about 45 per cent. Clinically all of these cases, except 8, are to be found

GROUP B.

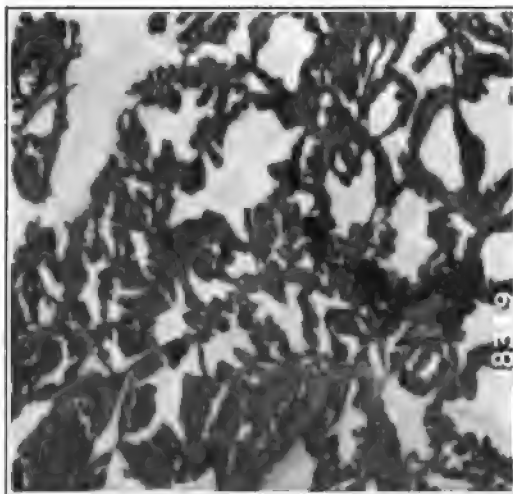


FIG. 11.—Photomicrograph.



FIG. 10.—Photograph of the thyroid gland.  $\times \frac{1}{6}$ .



FIG. 12.—Portrait before operation.



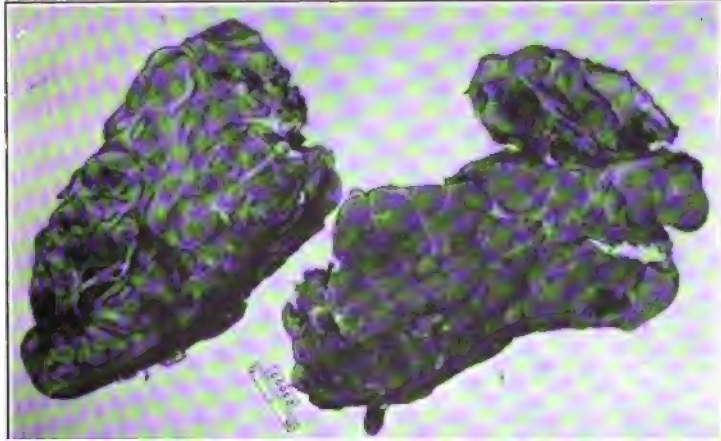


FIG. 13.—Photograph of the thyroid gland.  $\times \frac{1}{2}$ .

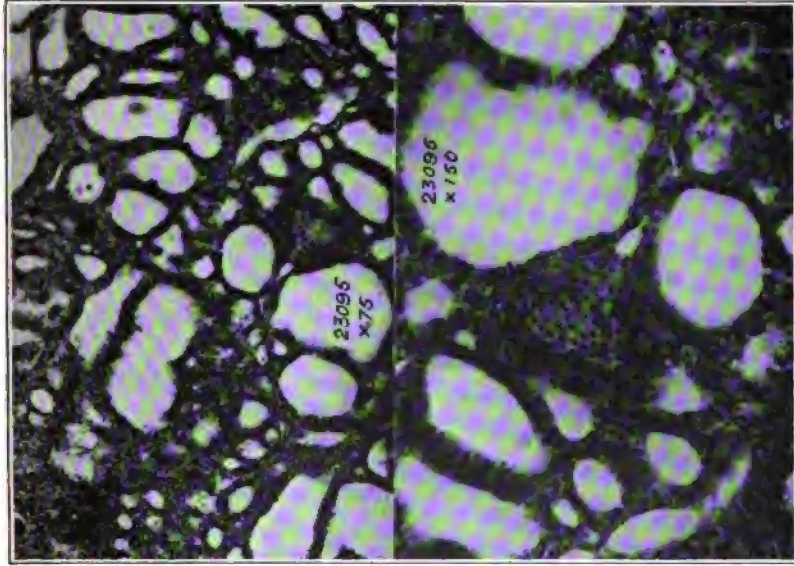


FIG. 14.—Photomicrographs.



FIG. 15.—Portrait before operation.



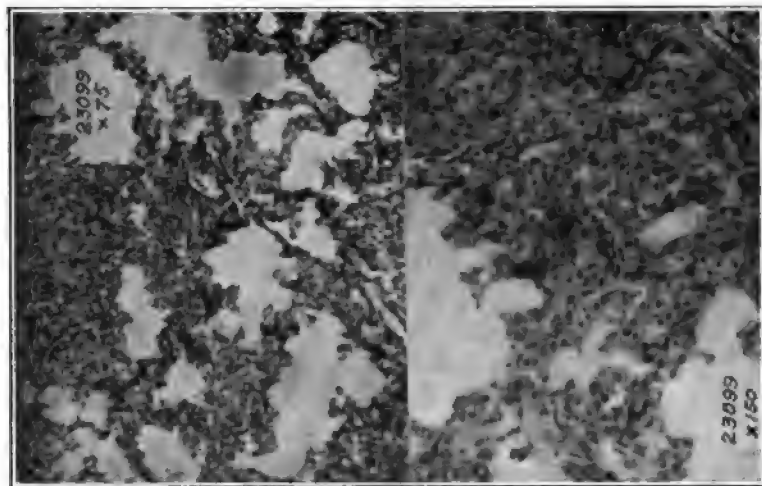


FIG. 17.—Photomicrographs.



FIG. 18.—Portrait before operation.



FIG. 16.—Photograph of the thyroid gland.  $\times \frac{1}{4}$ .





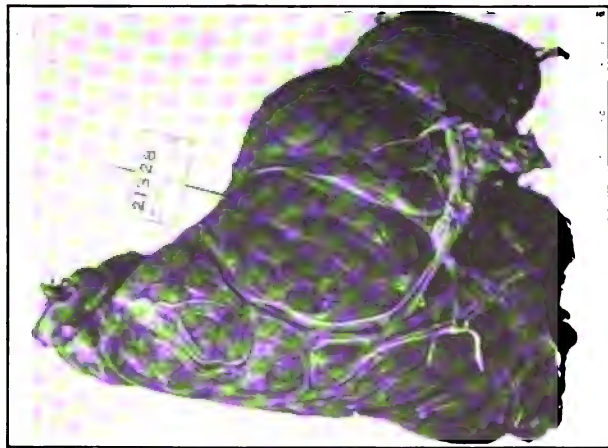


FIG. 19.—Photograph of the thyroid gland.  $\times \frac{3}{4}$ .

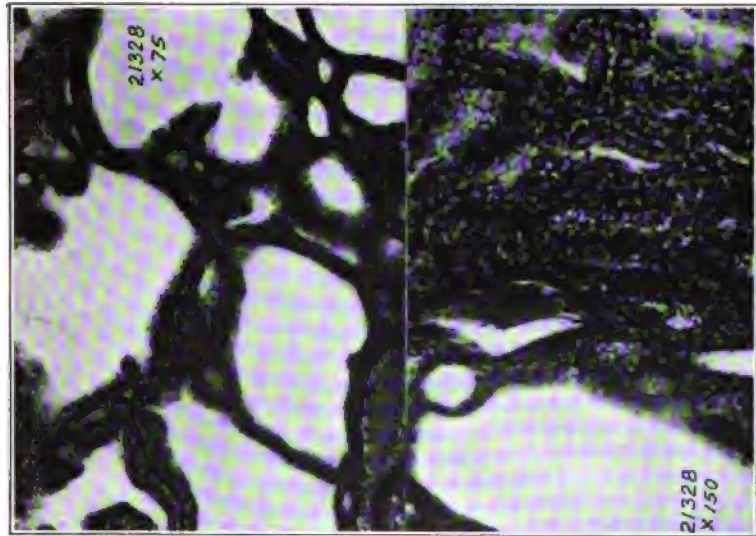


FIG. 20.—Photomicrographs.



FIG. 21.—Portrait before operation.



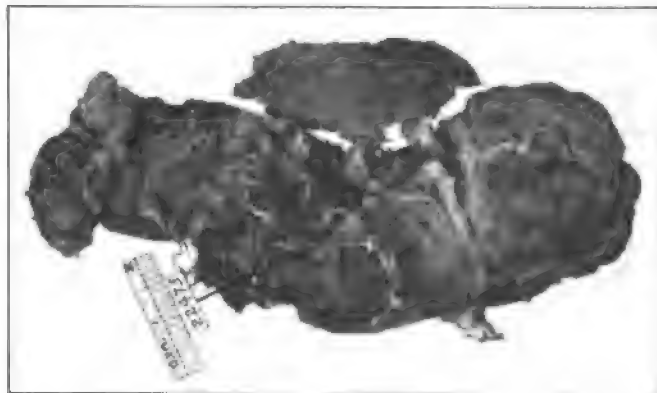


FIG. 22.—Photograph of the thyroid gland.  $\times \frac{1}{4}$ .

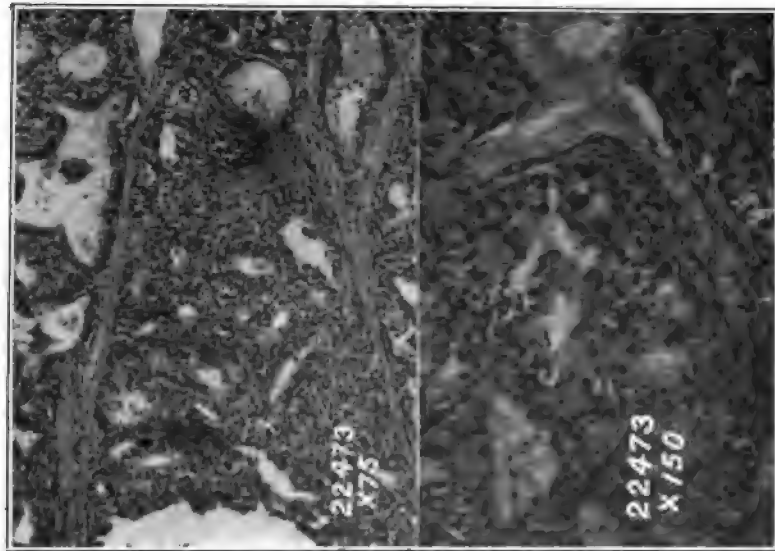


FIG. 23.—Photomicrographs.



FIG. 24.—Portrait before operation.





FIG. 27.—Portrait before operation.

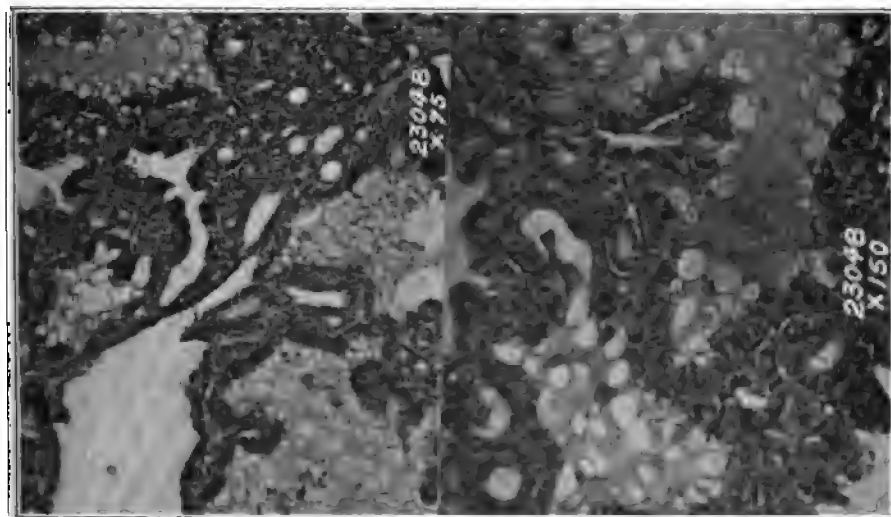


FIG. 28.—Photomicrographs.

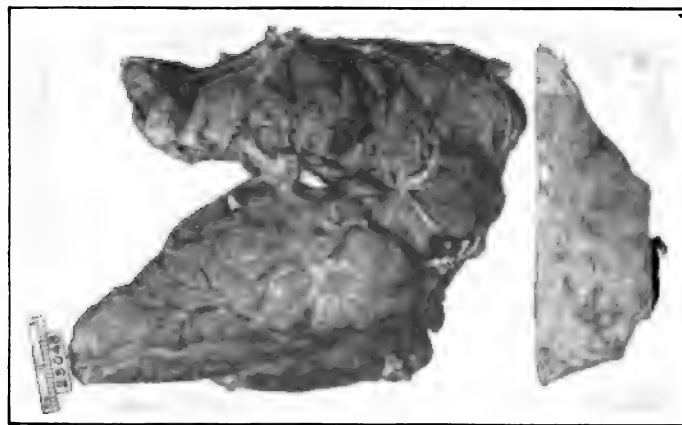


FIG. 25.—Photograph of the thyroid gland.  $\times \frac{1}{2}$ .



in the first, that is, acute stage of the disease, and all of them, of two, three, or four, degrees of severity; 7 of the remaining 8 cases had shown some remission of symptoms and they are counted in our series of partial disagreements.

The characteristics of this group may be stated as follows: 1. Large intra-alveolar parenchyma increase. Shown by: (a) Size of the gland; (b) increased number of cells in a single layer; (c) reduplication of layers; (d) infolding of alveolar walls; (e) papillæ formation. 2. Large amount of thin secretion. Shown by: (a) "Glair" of fresh section; (b) large amount of secretion which is non-eosin staining in stained sections.

**PATHOLOGICAL GROUP C.** Case No. 22,473 (Fig. 22).—This is a 35-gram gland whose granular, glairy, cut surface presents some alternating areas of gelatinous appearance. Histologically (Fig. 23) the large alveoli contain numerous papillary projections, but the columnar parenchyma cells are exfoliating in many areas. There is a large amount of secretion, much of which is non-staining, but some of which is stainable. Pathologically this case should show some remission over its previous symptoms. Clinically (Fig. 24) the patient is a woman, aged twenty-nine years, who for three years has shown symptoms of Graves' disease, which, although now of a severe type, are less severe than they have been previously.

Case No. 23,048 (Fig. 25).—This is a 45-gram gland, hard, nodular, with much of the cut surface granular, glairy, but in some areas gelatinous. Histologically (Fig. 26) there are large alveoli, great intra-alveolar parenchyma increase, papillæ formation, and a large amount of secretion, some of which is stainable and some unstainable. There is also considerable exfoliation of parenchyma and marked cytolysis in some areas. Clinically (Fig. 27) the patient is a female, aged thirty-seven years, who has had symptoms of Graves' disease for sixteen years. Although her present symptoms are now those of very severe hyperthyroidism they have been worse, and there have been numerous remissions during the period of her illness.

These cases illustrate pathological Group C. Clinically this group contains 54 of our cases, or about 21 per cent. These are almost all second-stage cases; that is, those showing more or less remission of previously severe symptoms, although even now they are of severe or very severe type.

The characteristics of this group may be stated as follows: 1. Large intra-alveolar parenchyma increase. Shown by: (a) Size of the gland; (b) increased number of cells in single layer; (c) reduplication of layers; (d) infolding of alveolar walls; (e) papillæ formation. 2. Large amount of thin secretion. Shown by: (a) "Glair" of fresh section; (b) large amount of secretion, most of which is non-eosin staining, in stained sections. 3. Beginning

degeneration. Shown by: (a) Denser staining of some of the secretion; (b) beginning exfoliation of the parenchyma.

**PATHOLOGICAL Group D.** Case No. 21,374 (Fig. 28).—This is a 200-gram goitre, hard and nodular externally, and with gelatinous cut surface. There is no markedly increased vascularity, while the stroma has materially increased. Histologically (Fig. 29) the alveoli are very large (0.6 to 1 mm.). There is almost complete exfoliation of the parenchyma cells, but the original character of the gland is definitely shown by well-preserved remains of papillæ in some of the alveoli. The secretion is very large in amount and well staining, being of the so-called "colloid" variety. If this represents a form of degeneration, the case should be one improved over its previous history. Clinically (Fig. 30) the patient is a woman, aged forty-four years, whose first Graves' symptoms developed about eight years ago. Although the condition of the heart makes the case still a severe one, yet the symptoms of hyperthyroidism are much reduced over what they were three years ago.

Case No. 21,756 (Fig. 31). This is a gland weighing 81 grams, whose cut surface is gelatinous throughout. Histologically (Fig. 32) the large alveoli contain well-staining secretion filled with the remains of exfoliated cells, and showing, in only a few instances, papillary projections sufficiently well preserved for identification. Clinically (Fig. 33) the patient is a female, aged fifty-seven years, who, for two years, until three years ago, had marked Graves' symptoms. Her present symptoms although mild are sufficiently well marked for diagnosis, although not enough to warrant operative interference, were it not for the pressure symptoms caused by the large gland. This is a case of self-cured Graves' disease, with the exception of the rapid heart and choking sensations.

These cases represent pathological Group D. There are 34 cases in this group, or 12 per cent. Clinically all of them are in the second or third clinical stages; that is, they show marked total improvement, or, at least, some cessation of the symptoms of acute hyperthyroidism. Many of them are still of two to four degrees severity.

The characteristics of this group may be stated as follows: 1. Old intra-alveolar parenchyma increase. Shown by: (a) Size of the gland; (b) remains of infolding; (c) remains of papillæ. 2. Large amount of thick secretion. Shown by: (a) Gelatinous appearance of fresh section; (b) large amount of secretion, most of which is eosin staining, in stained sections. 3. Advanced degeneration. Shown by: (a) dense staining of most of the secretion; (b) more or less complete exfoliation of the parenchyma.

**PATHOLOGICAL GROUP E.** Case No. 21,964 (Fig. 34).—This is an 88-gram gland, hard and nodular externally, and showing small



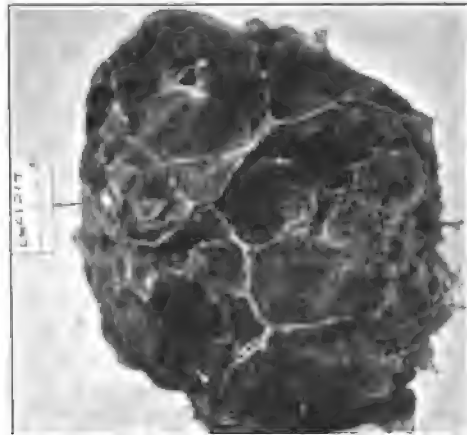


FIG. 28.—Photograph of the thyroid gland.  $\times \frac{1}{6}$ .



FIG. 29.—Photomicrograph.



FIG. 30.—Portrait before operation.





FIG. 33.—Portrait before operation.

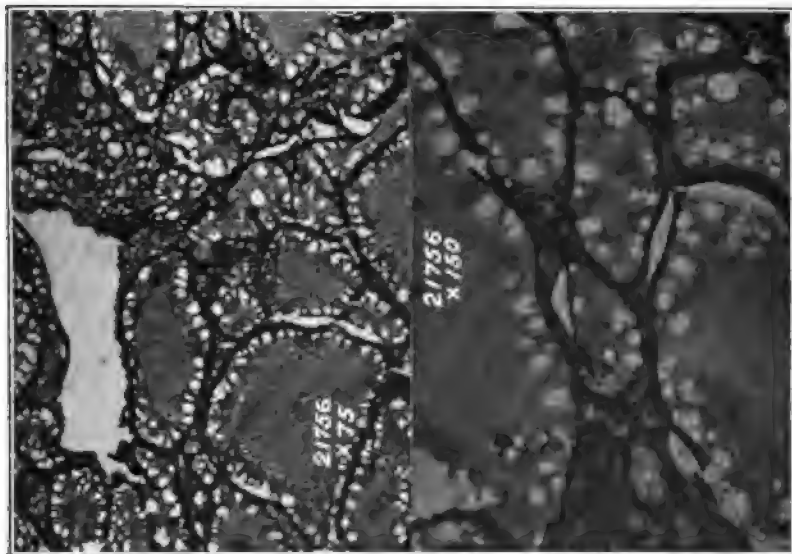


FIG. 32.—Photomicrographs.

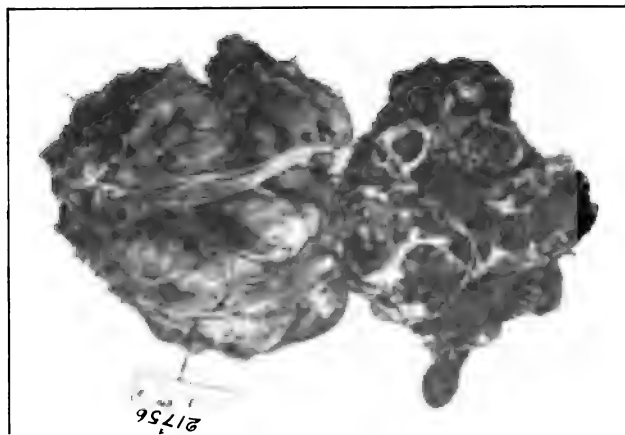


FIG. 31.—Photograph of the thyroid gland.  $\times \frac{1}{2}$ .



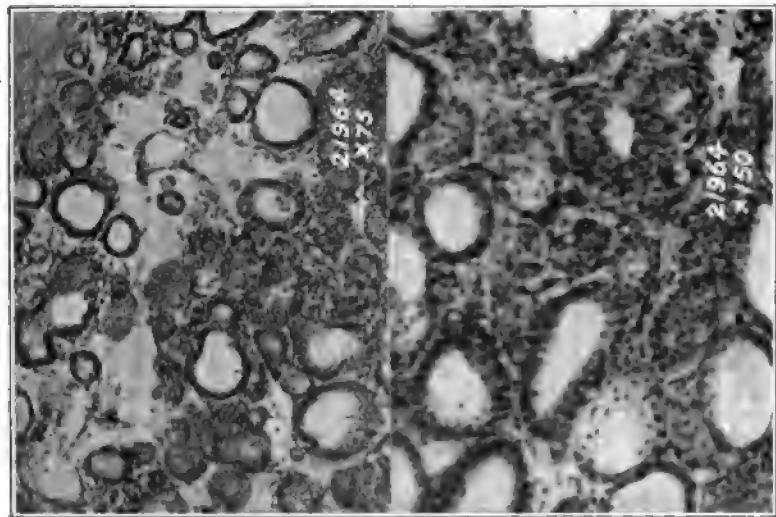


FIG. 35.—Photomicrographs.

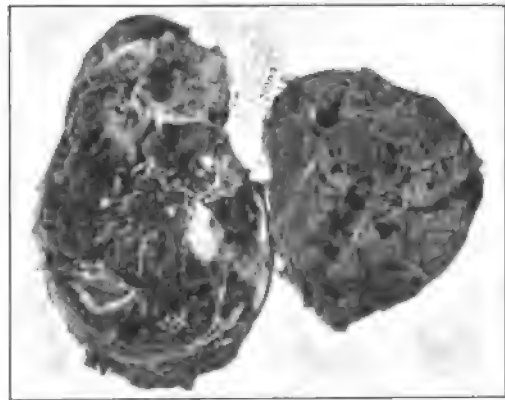


FIG. 34.—Photograph of the thyroid gland.  $\times \frac{1}{4}$ .



FIG. 36.—Portrait before operation.





FIG. 39.—Portrait before operation.

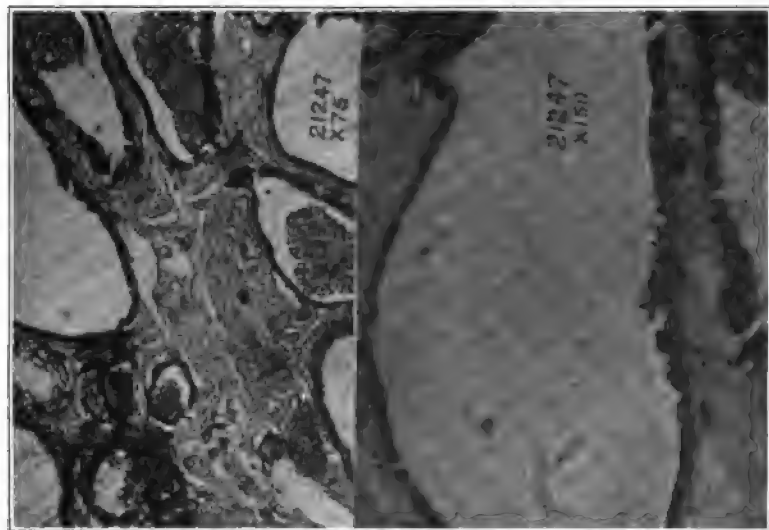


FIG. 38.—Photomicrographs.



FIG. 37.—Photograph of the thyroid gland.  $\times \frac{3}{4}$ .







FIG. 40.—Photograph of the thyroid gland.  $\times \frac{3}{4}$ .

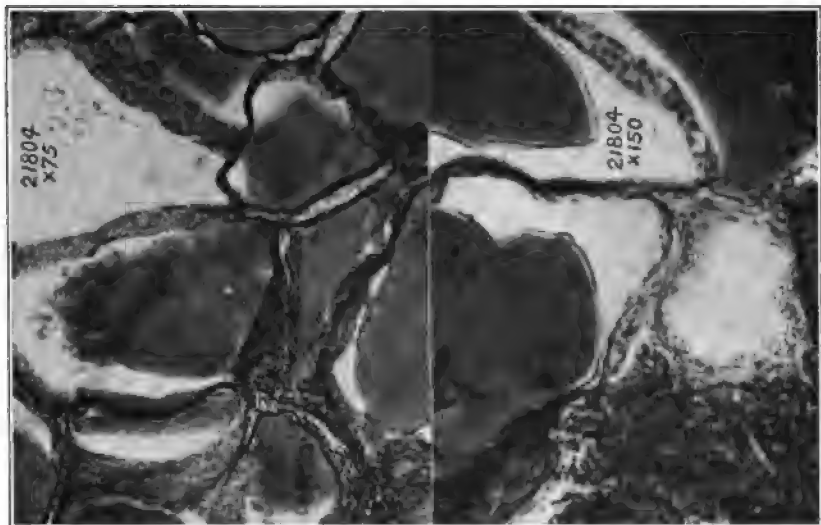


FIG. 41.—Photomicrographs.



FIG. 42.—Portrait before operation.



cysts on its cut surface, which is otherwise dry and rather solid looking. Histologically (Fig. 35) the alveoli are found to be quite small (from 0.05 to 0.08). This is a typical proliferating adenoma of foetal type. There is only a small amount of thin non-stainable secretion. Clinically (Fig. 36) the patient is a female, aged thirty-three years, who had a slowly developing gland for six years, with Graves' symptoms coming on so slowly that they caused no disturbance until two years ago, and even now they are only moderately severe.

This case represents the first pathological group (Group E) of the second series. The first series, Groups A, B, C, and D are essentially an intra-alveolar form of parenchyma increase, while these show multi-alveolar parenchyma increase; that is, they resemble adenomas in type. There are but 11 cases, 4 per cent., of this type in our series. Clinically all of them are mild, continuous cases of Graves' disease of from one to thirteen years' duration. All of them are of moderate severity, and were operated upon, as much on account of pressure symptoms, as because of hyperthyroidism, although the latter was sufficiently pronounced to render the diagnosis unmistakable.

The characteristics of this group may be stated as follows: 1. Small multi-alveolar parenchyma increase. Shown by: (a) Size of the gland; (b) recently formed alveoli. 2. Small amount of thin secretion. Shown by: (a) Dryness of fresh section; (b) small amount of secretion, which is non-eosin staining, in stained sections.

**PATHOLOGICAL GROUP F.** Case No. 21,247 (Fig. 37). This is a 70-gram gland which is rather soft, and on gross-section collapses readily, although it contains no definite cyst. Histologically (Fig. 38) the specimen is adenomatous in type, with considerable parenchyma increase and a large amount of non-stainable secretion. Clinically (Fig. 39) the patient is a woman, aged thirty-seven years, who for one year has had an enlarged thyroid, nervousness, profuse sweating, and fine tremor. She would be classed as in stage one or mild continuous and of grade 1 in severity.

This case represents pathological Group F, which is the same as Group E except that the glands show a greater parenchyma increase and contain a larger amount of thin secretion in the alveoli. There are but 5 cases of this group, or 2 per cent., in our series.

The characteristics of this group may be stated as follows: 1. Large multi-alveolar parenchyma increase. Shown by: (a) Size of the gland; (b) recently formed alveoli. 2. Large amount of thin secretion. Shown by: (a) "Glair" of fresh secretion; (b) large amount of secretion, which is non-eosin staining, in stained sections.

**PATHOLOGICAL GROUP G.** Case No. 21,804 (Fig. 40). This is a 42-gram gland, gelatinous on its cut surface and with rather large alveoli (Fig. 41) filled with stainable secretion and showing con-

siderable exfoliation of its parenchyma. Clinically (Fig. 42) the patient is a female, aged twenty years, who has had mild Graves' symptoms for a year and one-half; that is, goitre, nervousness; pulse has been 180, is now 130; menstruation has not been disturbed. One year after her operation her return history shows her to be well.

This case represents pathological Group G of which there are 11 cases, or 4 per cent., in our series. All of these are mild continuous of but moderate severity (Grade 2).

The characteristics of this group may be stated as follows: 1. Large multi-alveolar parenchyma increase. Shown by: (a) Size of the gland; (b) recently formed alveoli. 2. Large amount of secretion. Shown by: (a) Large amount of secretion, most of which is non-eosin staining, in stained sections. 3. Beginning degeneration. Shown by: (a) Denser staining of some of the secretion; (b) beginning exfoliation of the parenchyma.

**PATHOLOGICAL GROUP H.** Case No. 23,724 (Fig. 43). This is a 55-gram gland whose cut surface is gelatinous and filled with cysts. Histologically (Fig. 44) the alveoli are large (from 0.2 to 0.5 mm. in diameter) and of adenomatous type. There is marked exfoliation in most areas. The secretion is large in amount and well stained. Pathologically this is an old adenomatous proliferation producing mild, exophthalmic symptoms. Clinically (Fig. 45) the case is a female, aged fifty-two years, who had had an old goitre for seventeen years. Within the last three years she has developed moderately severe symptoms of Graves' disease which have been at a stand-still for the past year.

This group represents pathological Group H. It contains 24 cases, or about 10 per cent. of the series. Clinically they are all mild, continuous or first-stage cases, and none are of more than moderate severity (Grade 2).

The characteristics of this group may be stated as follows: 1. Old multi-alveolar parenchyma increase. Shown by: (a) Size of the gland; (b) sometimes scattered groups of recently formed alveoli. 2. Large amount of thick secretion. Shown by: (a) Gelatinous appearance of fresh section; (b) large amount of secretion, most of which is eosin staining, in stained sections. 3. Advanced degeneration. Shown by: (a) Dense staining of most of the secretion; (b) more or less complete exfoliation of the parenchyma.

On the basis of the above pathological grouping, which was made originally without reference to clinical conditions and without knowledge of the clinical facts in any of the cases, I ventured a conjecture as to the probable clinical history in each case. Aside from the pathological data this conjecture was based on the working hypothesis that the severity of the symptoms in Graves' disease is probably directly proportional to the amount of thyroid secretion



FIG. 45.—Portrait before operation.

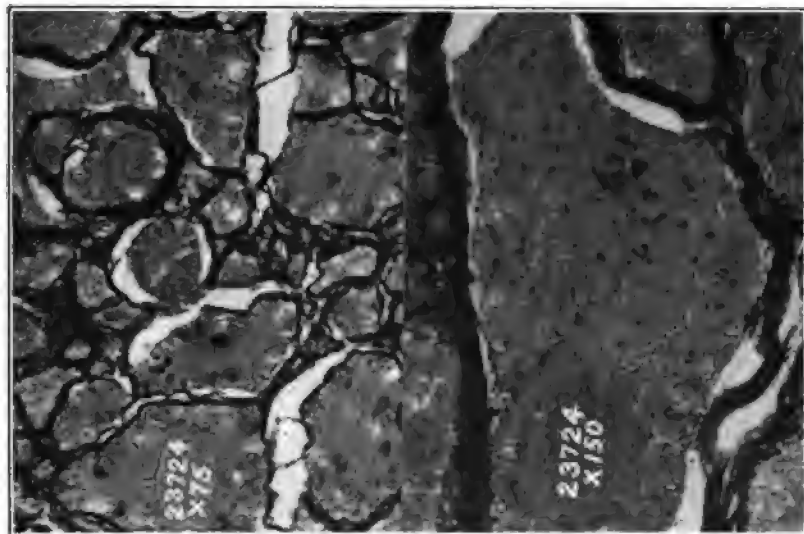


FIG. 44.—Photomicrograph.

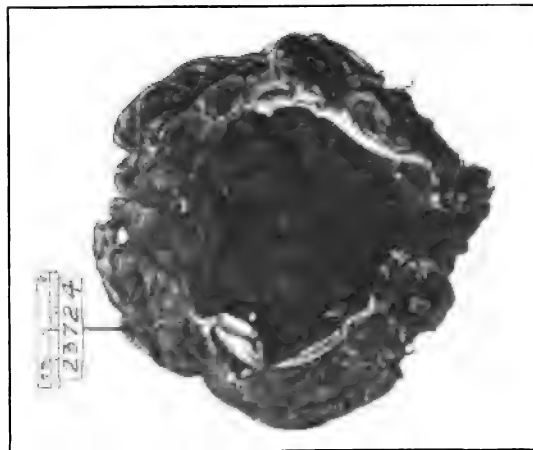


FIG. 43.—Photograph of the thyroid gland.  $\times \frac{1}{2}$ .



absorbed from the glandular alveoli. The whole study was an attempt to determine, in as unbiased a manner as possible, whether or not any such definite relationship really exists between the varying pathological changes in the thyroid gland and the varying symptoms in Graves' disease.

For finally determining the value of these conjectures the following method was adopted: Dr. H. S. Plummer, who had written the original office histories in the majority of the cases, kindly reviewed his own histories as well as those of the other clinicians, and grouped them as follows: Grade 1: Acute cases of (1) mild, (2) moderate, (3) severe, or (4) very severe degree. Grade 2: Cases which had been severe, but at the time of examination showing remission of symptoms. Grade 3: Cases of previously severe hyperthyroidism, but with symptoms now chiefly of severe vital-organ-lesion type (heart, nervous system, etc.), rather than hyperthyroidism. Grade 4: Mild, continuous cases, slowly developing.

When the clinical and pathological classifications had been definitely made, the two were compared case by case. As a result an almost complete parallel was found to exist between the pathological conjectures and the clinical facts in about 80 per cent. of the cases. In about 17 per cent. more the apparent disagreements were readily explicable on reviewing both the clinical and the pathological data. In but 6 of these cases, or less than 3 per cent., there was a disagreement for which, as yet we have been unable to find any positive explanation. In these 6 cases the pathology indicates a more severe type of the disease than is shown by the clinical histories.

Having found that the pathological groups in our series of cases correspond with considerable accuracy to well-marked clinical groups, it is necessary to examine them a little more closely to determine, if possible, what this correspondence may indicate in regard to the pathological development. It will be noted that the groups are in two series: (1) Those essentially with increased parenchyma within alveoli, and (2) those with increased number of alveoli. Each series starts with a group, with but a small amount of parenchyma and secretion increase (A and E), proceeds to a group with a large amount of parenchyma and secretion increase (B and F), and thence to a group like the preceding, with but beginning degeneration (C and G), and terminates with a group characterized by more or less complete degeneration (D and H).

As suggested above the clinical interpretation of this grouping is made on the following working hypothesis, which is merely an elaboration of Möbius' theory:

1. That the symptoms of Graves' disease are associated with increased absorption of an increased secretion of the thyroid gland.
2. That the more functioning parenchyma cells in the gland the larger the amount of its secretion.

3. That the more fluid the secretion of the gland the more readily will it be absorbed.

4. That the cells partly disintegrated and found embedded in the secretion in the alveoli with partially or wholly naked walls are mostly, if not entirely, desquamated epithelial cells.

5. That the increased concentration of the stained secretion by the absorption of its own fluid constituents and by the desquamation of the alveolar epithelium, probably tends to reduce absorption from the gland as a whole.

6. That the dense, gelatinous, well-stainable secretion, the so-called "colloid" in any thyroid gland is not, probably, strictly speaking, a normal product, but the complement of the absorbed portion.

7. That when dense, basic-stained, colloid material fills the alveoli of the thyroid gland it probably should be regarded as evidence, not of present secretion, but of blocked absorption and parenchyma destruction.

8. When, therefore, we measure either histologically or chemically, the relative colloid (globulin) content of the thyroid gland, we should bear in mind that we are probably not determining factors which have actually caused the symptoms, but only their associated phenomena.

On such a basis a very simple hypothesis of the development of Graves' disease may be formulated as follows:

1. Following a metabolic, chemical, or extra-organismal irritant, thyroid parenchyma proliferates, over-functionates, and degenerates.

2. This process primarily resembles simple, adenomatous proliferation, or reminds one of adenopapilloma.

3. Either process may start in a gland not previously enlarged by retained secretion, or in one which is already distended with non-absorbed secretion.

4. The severity of the symptoms depend upon (a) the amount of absorbable secretion, and (b) the patient's ability to neutralize the secretion.

I would urge that, in making histological examinations of the glands from cases of hyperthyroidism, the gland should be studied throughout, and that the statement of findings in such cases should express the observer's estimation, not of what was found in this or that area in the gland, but rather of the total secretory power and amount of absorbable material in the gland.

While our cases are too few from which to draw positive conclusions, yet so far as they go they seem to warrant us in making the following tentative statements from the clinical standpoint:

1. Very early acute cases show pathologically hyperemia and cellular hyperplasia, if not throughout the gland, at least in much of it, providing, of course, the more enlarged lobe has been removed.

2. Later acute, moderate, severe, and very severe cases show



greater parenchyma increase, and in many instances evidence of increased absorbable secretion. Speaking broadly the parenchyma increase is in direct proportion to the intensity of the symptoms. The relatively few variations from this rule may be accounted for by the varying resisting power of different individuals. When relatively small amounts of absorbable secretion are found in alveoli whose walls are crowded with actively functioning cells, we may fairly assume that the secretion has already been absorbed.

3. Cases which clinically are showing any remission of toxic symptoms, show somewhere within the gland more or less evidence of decreased function in the exfoliation or marked flattening of parenchyma cells, or of probably decreased absorption, by the presence of thick, gelatinous, stainable secretion, the so-called "colloid."

4. Patients who have recovered from their toxic symptoms and are now suffering principally from long, previously acquired heart or nerve lesions, or from myxoedema, although no myxoedema cases are included in our present list, show exfoliated or much flattened (probably non-secreting) epithelium and large quantities of well-stained, thick, gelatinous, probably non-absorbable, colloid. In this class of cases it seems as futile to search for previous, causative parenchyma increase as to look for diphtheria membrane in the throat of a patient suffering from post-diphtheritic paralysis.

5. The recently developed, very mild, or moderately mild, cases of long standing show pathologically almost always some total parenchyma increase by the multiplication of alveoli, but apparently not greatly increased functioning power of the individual parenchyma cells. Goitres of the adenoid type (Groups E, F, and H) apparently pass through the same changes of hypertrophy and degeneration as those of the papilliferous type (Groups A, B, C, and D).

6. Simple goitres should be regarded as multiple retention cysts filled with non-absorbable secretion, cell detritus, etc.

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## INFERIOR POLIO-ENCEPHALITIS IN A CHILD OF FOUR YEARS, WITH RECOVERY.

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A BOY, aged four years, was admitted to Dr. Judson's service in St. Christopher's Hospital, October 29, 1907, and presented an

unusual combination of symptoms. His family history was negative. He had been healthy from birth and had not had any infectious disease. Three weeks before his admission to the hospital the mother noticed that he was "stiff" (as she described it) on coming down stairs in the morning, and thought that he had rheumatism, because he seemed "stiff and sore." After breakfast, however, the child played about outside as usual. The mother soon noticed that he staggered and that his right eye was turned inward. He held his head to the right side, although he was able to move it in all directions. He continued to play about, but seemed dull. During this time he had a cold and a paroxysmal cough. He never had any convulsions, did not complain of pain or headache, did not vomit, ate well, voided his secretions normally, and did not appear feverish. It is questionable, however, whether he did not have a slight rise of temperature. The mother failed to notice any weakness of his extremities. He was particularly stupid just before he was brought into the hospital, and staggered a great deal on the way there.

The examination of the boy showed him to be well developed, and of good color. There was a slight scalp wound in the left temporal region, from a fall on the sidewalk five weeks before his admission. His throat was clear. His lungs, heart, and abdomen were normal. The spleen was not palpable, the liver barely so. The lymphatics and the epiphyses of the long bones were not enlarged.

The mental condition of the child was very dull, and he had incontinence of urine and feces. There was no loss of power in the extremities, and the grip was good. There was no wasting. Measurements showed both sides to be equal. The electrical reactions were normal. There was a marked ataxia of the cerebellar type, and Romberg's sign was present. The knee-jerks and Achilles jerks were absent. The skin reflexes were normal. There was no Babinski and the normal plantar reflex was obtained. There were no sensory or trophic disturbances and the tactile, pain, and temperature senses, as well as the sense of position, appeared normal. There was a coarse tremor of the hands when the patient was disturbed. Coördinate movements were well performed when the child was in the recumbent position. In addition to the mental hebetude, incontinence, cerebellar ataxia, and loss of deep reflexes, there was paresis of both external recti, more marked on the right side, with deviation of the tongue to the left and an extremely slight obliteration of the nasolabial fold on the left side. The other extra-ocular muscles acted normally, and the pupils were equal, reacted to light, and accommodated freely. The eye-grounds were examined by Dr. Kraus, and found normal. Dr. Stimson found hearing equal and normal on both sides, with a normal tympanum. Four examinations of the urine gave negative results. On November 9, 1907, an ounce of clear cerebrospinal fluid was withdrawn by lumbar puncture, but this failed to present abnormal features. No

cellular elements were found. The temperature showed slight elevation on admission and this persisted for two weeks. The average was from 99° to 100°. It then gradually dropped to the normal line. The pulse ran from 100 to 120, and the respiratory rate from 25 to 30.

A few days after admission the patient became a little brighter, and a week after admission the paresis of the external recti was less marked. There was at this time also only an occasional incontinence of urine and no longer any tremor. The boy continued to grow brighter, and on November 22 the ocular palsy was much improved. The tongue at this time was still slightly deviated to the left. The ataxia persisted and the deep reflexes remained absent. His condition continued practically unchanged until his temperature again rose, in the first week in December, when an uneventful attack of typhoid fever set in, and lasted a little over three weeks.

An analysis of the case quickly shows that we were dealing with motor symptoms confined to the functions of three different cranial nerves; the twelfth on the left side, both sixths, and possibly the left seventh (the latter was extremely slight). The involvement of the sixth was very much more marked on the right side, while the twelfth was affected on the left. Other motor involvement there was none, and the only additional symptoms to help localize were the ataxia and loss of deep reflexes.

A single circumscribed lesion would not account for the combination of symptoms; for the sixth nucleus was much more markedly involved on the right side, while the involvement of the twelfth nerve nucleus was on the left. We were, without doubt, dealing with a pathological condition in the lower part of the pons and the upper part of the medulla: it would be almost impossible to account for the symptoms by pressure from elsewhere, such as a tumor of the cerebellum, since that could hardly press upon the hypoglossal and facial with more marked pressure on the sixth of the opposite side, and this without affecting the pyramidal tracts. As the child failed to present other usual symptoms of cerebellar tumor, such as optic neuritis and vomiting, that diagnosis was excluded. His subsequent complete recovery confirmed this opinion. There was no evidence of meningitis at any time.

We were then obliged, by the combination of the paresis of these few cranial nerves and the cerebellar ataxia, to locate the disease in the pons and medulla. There was no history of syphilis or tuberculosis, and the boy had been a particularly healthy child. A thrombosis or embolism could not be accounted for, as there was no cardiac or arterial disease. The child showed no evidence of syphilis. Furthermore we could not assume that there was a hemorrhage into the pons caused by the violent straining of a whooping-cough. Also, as the condition did not come on suddenly, a hemorrhage was extremely unlikely. Therefore, we were forced to think of polio-

encephalitis, for there was irregular involvement of a few motor cranial nerves whose nuclei are closely related by position in the lower pons and upper medulla; and the derangement of functions did not extend to the ventral portion of the pons, but left the pyramidal tracts apparently uninvolved.

The course of the disease, with mild febrile disturbance and the marked mental hebetude, which at one time after the boy's admission to the hospital approached stupor, confirmed the diagnosis of polio-encephalitis. The disorder also developed at the end of an epidemic of poliomyelitis, which occurred in Philadelphia and in other parts of Pennsylvania in the autumn of 1907.

The modified views of Strümpell<sup>1</sup> (whose earlier conception of encephalitis as a process involving the cortical area alone, was not concurred in) have been confirmed and it is now an accepted fact that a certain number of cases of cerebral palsy are due to acute non-suppurative encephalitis. The presence of this morbid state has been demonstrated by the pathological findings of Ganghofner, Sachs, and Fischl at least; and the simultaneous appearance of such foci of disease in the brain with the lesions of acute anterior poliomyelitis has been observed by Redlich and others. A number of cases of acute anterior poliomyelitis in the adult accompanied by inflammation in the medulla, pons, crura, cerebral ganglia, or cortex have been studied pathologically. Such was a case in an adult reported by Sherman and Spiller<sup>2</sup> in 1900. As a result of his studies Spiller concludes that "poliomyelitis is closely related pathologically to the non-purulent form of encephalitis, and to the polio-encephalitis superior of Wernicke," and that "poliomyelitis in the adult is essentially the same disease as poliomyelitis in the child."

Any part of the brain can be the seat or point of origin of this trouble. After referring to the frequency with which the central ganglia alone are affected, Oppenheim<sup>3</sup> concludes that the gray matter in the wall of the third ventricles and the aqueduct of Sylvius is the seats of predilection, whence the disease may descend to the spinal cord, that involvement of the cerebellum is less frequent, that the process may extend to the optic nerves and retina, that as a rule there are several foci, and, that although the gray matter is principally involved, the disease may extend in the neighboring white matter.

In this connection it is well to call attention to the fact that the pathological findings in anterior poliomyelitis have shown that the inflammatory changes are really a myelitis principally limited to the gray matter of the cord, particularly the anterior horns, but that the other adjacent portions of the white matter, or even the

<sup>1</sup> Practice, thirteenth edition.

<sup>2</sup> Oppenheim in Nothnagel's System.

<sup>3</sup> Phila. Med. Jour., November, 1900.

membranes, do not entirely escape. That the cause acts through and upon the bloodvessels and does not pick out the anterior horn cells and leave the surrounding tissue unaffected, has been established in spite of the fact that the clinical manifestations point to the anterior horn cells alone. Oppenheim also says: "It is not infrequent to find a single circumscribed process within the pons and medulla, but the size and extent of any focus may vary in wide limits." We think that our case gave evidence of the presence of inflammatory changes in the lower part of the pons, creeping slightly into the medulla on the left side (judging from the clinical signs), and that the lesion was due to an encephalitis. Polio-encephalitis may run an acute or subacute course, and, although in severe types it may end in death within two or three weeks, it is capable of ending in complete or partial recovery and this in cases of more extensive involvement than ours. Comby<sup>4</sup> and Medin report cases which recovered without any remaining paralysis. Abt,<sup>5</sup> of Chicago, reports two recoveries with residual paralysis. Frederick Taylor,<sup>6</sup> of London, records a case of encephalitis which recovered after a prolonged period of ataxia lasting over three years.

Our case, which was rather mild, ran six weeks (the rise of temperature lasting only two) with decided improvement, when the temperature again rose and a mild attack of typhoid fever set in, during the course of which there were no new nervous manifestations. Upon complete recovery from the typhoid the ataxia had entirely disappeared, as well as the cranial nerve palsies. The last symptom to disappear was the absence of the tendon reflexes, but by February 1908, the knee-jerks, although somewhat weak, were unmistakably present.

Pathological study of the lesion shows that there is cellular infiltration, which may or may not be intense, and is particularly marked along the vessels and in the perivascular sheaths. The vessels are engorged and there are frequent hemorrhages. The cellular infiltration may be marked in the nuclei. The nerve cells and neuroglial tissue may be, in the beginning, swollen, or the nerve cells may be shrivelled, with a disappearance of their dendritic processes, and lack of distinct nuclei. They may ultimately disappear. The essential pathological process in encephalitis is the breaking down of the nervous elements, and extensive granular degeneration. From a number of observations in which the complete function of the nerves was restored, it seems that the lesions produced by encephalitis may be completely absorbed with a restoration to the normal condition, or there may be local necroses or softening, or the focus may be obliterated by connective-tissue formation.

When we come to infer the pathology of a case such as ours (of

<sup>4</sup> Archives de médecine des enfants, 1907.

<sup>5</sup> Archives of Pediatrics, May, 1907.

<sup>6</sup> Lancet, 1904, ii.

the inferior type) it is well to remember that the inflammation may extend farther than the clinical signs indicate.

It is difficult in a short space to give any summary of the symptoms of this disease, because they are so varied in their combinations. The process may begin above, starting for instance, with the oculomotor region, and go down finally causing atonic paralysis of the extremities; or, on the contrary, it may begin below and travel upward, presenting the course of Landry's paralysis. In typical cases only motor functions are involved. There may be different combinations, more or less symmetrical, of paralysis of the cranial and motor spinal nerves. When the cranial nerves are involved, there may be ophthalmoplegia and glossopharyngeal-labial paralysis. Thus the signs of bulbar disease may be difficult articulation, swallowing, or breathing. A hemiplegia may accompany the other symptoms. The disease in its acute manifestations may be initiated by headache, vertigo, nausea and vomiting, fever, general weakness, and more or less stupor. Its onset, though often very rapid, is, on the other hand, not apt to be as sudden as in hemorrhage, and the fact that it may develop through days or weeks is a diagnostic point in favor of encephalitis against hemorrhage. Stupor may deepen to loss of consciousness, with restlessness and delirium, and there may be general convulsions and retraction of the head. Paralysis occur early, but may not at first be apparent. Not infrequently the pulse is slow, but the respiration is apt to be rapid.

The combination of palsies in polio-encephalitis inferior is very variable, and a search of the literature has revealed a very limited number of cases resembling the one here reported. In a case of Leyden's, a boy, aged fifteen years, there was difficulty in swallowing, rigidity of the neck, ataxia, paralysis of both facials, of the hypoglossals, and of the soft palate and vocal cords; later also paralysis of the sixth nerves. The disease lasted eleven days, and the autopsy showed an encephalitis in the region of the medulla.

Dinkler<sup>7</sup> (from Erb's clinic) reports a case of acute inferior hemorrhagic polio-encephalitis of wide extent. A healthy child, aged two and a quarter years, fell down a flight of stone steps, receiving a slight scalp wound, and was unconscious a short period without vomiting or convulsions. After this he was altered psychically, had headache, vertigo, enuresis, occasional vomiting, and a very staggering gait. These symptoms lasted two and one-half years, when, after a vomiting attack, speech became affected, chewing and swallowing difficult, and great restlessness set in. The child died, after two feverish days, in deep coma. The gray substance of the medulla, the posterior horns of the cervical cord, and the floor of the fourth ventricle showed recent bloody extravasations with changes and rupture of the bloodvessel walls. Although the last eight pairs of

<sup>7</sup> Deut. Ztschr. f. Nervenheilkunde, 1895, vii.

cranial nerves were thus surrounded the author says they suffered practically no destruction, because death occurred from intracranial pressure before there was time for this to take place.

The following is a case of Batten's\*: A child of five years was taken ill with fever, and two days later suddenly developed a right-sided facial palsy, with difficulty in swallowing due to weakness of the right side of the palate. There was no paralysis of limbs or eye muscles. Vomiting was present, but there was no loss of consciousness. Death occurred three days later from respiratory failure. There was complete destruction of the right seventh nucleus, in the region of which there were hemorrhages, thrombosis of smaller vessels, and round-cell infiltration. The engorgement of the vessels produced apparently little change in the left seventh or either of the sixth nuclei. There was also considerable vascular engorgement with exudation of round cells in the medulla in the region of the ninth, tenth, eleventh, and twelfth nuclei, without destruction of these. There was perivascular exudation in the gray matter of the upper cord. Batten remarks that the lesion was of vascular origin and exactly corresponded in appearance with that found in an acute anterior poliomyelitis and in acute polio-encephalitis superior. He alludes to the fact that the former disease occurred frequently during the preceding August, and considers this case to be of the same nature.

The cause of polio-encephalitis, excluding alcoholism, which is responsible so frequently for the Wernicke type of the disease, is mainly the infections and especially influenza. But such an infection was absent in our case. We are in the dark, however, as to the specific cause of anterior poliomyelitis, which so often occurs in epidemics, and the case herewith reported appeared at the end of a severe epidemic of poliomyelitis. It seems hardly justifiable to regard the fall that the child sustained, five weeks before his entrance to the hospital, as an etiological factor. It was only on the pavement while he was playing in the street, and there were no symptoms of concussion; he never became unconscious and was unchanged after this tumble until the disease began two weeks later. He had been in the hospital four weeks when his typhoid developed, so that no claim can be made of any causal relation between the two affections. The total duration of the disease was about three months, since there was no ataxia nor any trace of the palsies upon his return, at the end of January, from the country, where he had been sent for a fortnight's convalescence.

We think this case is of interest because it forges one more link in the chain that unites poliomyelitis and non-suppurative encephalitis, because it shows the inferior type of polio-encephalitis, because it illustrates that this disease may run a comparatively mild course to complete recovery, and from the fact that it followed an epidemic of poliomyelitis.

\* *Lancet*, October and December, 1902.

**THE GONOCOCCUS AS A FACTOR IN INFECTIONS FOLLOWING  
ABORTION OR FULL-TERM DELIVERY.**

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PROBABLY no subject of equal importance in medical science shows such diverse opinions as that regarding the cause and means of prevention of infection following the discharge of the products of conception from the uterus. Since Mayrhofer in 1863, Coze in 1869, and more especially since Pasteur in 1879, found the streptococcus in the lochia of women suffering from puerperal fever, this organism has been looked upon as the most important bacteriological factor in this disease. In consequence the attention of numerous investigators has been directed toward the presence of this coccus in the vaginal discharge of pregnant and non-pregnant women. The results of examination have not been uniform, and opinion has been varied regarding the possibility of auto-infection and the value of antepartum douches. Although many observers have proved the prevalence of gonorrhœa in modern society, few have been able to show that it is of definite importance in the production of more important forms of puerperal fever.

Experiments by Duhrssen, Bumm, and others, as well as my own observations appear to prove that the normal vaginal, cervical, and urethral epithelium is not attacked by the ordinary pyogenic cocci. When, however, the resistance of the parts is overcome by such an organism as the gonococcus, other bacteria seem able to produce their characteristic lesions. This fact, I believe, is of importance in our consideration of postpartum infections and will help, in part, to explain the diverse opinions held by various authorities upon the question of auto-infection.

The number of cases in my series is small; the results, however, are very suggestive. I believe that the careful examination of the lochia at the onset of fever would demonstrate the gonococcus in a large number of cases. It does not seem unreasonable to suppose that the streptococcus and other pathogenic organisms, which are constantly present in the rectum and the external genitals, should be ready to invade the vagina whenever an opportunity is given. The gonococcus present in the cervical glands or other part of the genital tract takes advantage of the bruised condition of the tissues after labor and sets up an inflammatory process. This process paves the way for a secondary infection by more pathogenic organisms, such as the streptococcus. These secondary invaders having gained entrance, the disease becomes more serious and presents graver symptoms.



The mortality figures of hospitals, in other ways of equal merit, do not materially differ whether douches are used during the latter days of pregnancy or not. At the same time, although the installation of aseptic methods has enormously reduced the mortality from puerperal infection, there still persists a certain number of cases occurring year by year. Many of these cases occur in women in whom labor has been spontaneous or even precipitate. Again, the mortality rate does not give an adequate idea of the incidence and importance of puerperal fever. Many patients are only saved after the most careful nursing and constant attention. Others after a severe illness for a few days are apparently cured and leave the hospital well. A still larger class run a mild fever for two or three days and are discharged after an otherwise normal puerperium. It is women of these classes who return within a few weeks or months to consult the gynecologist for inflammation of the uterine appendages, pelvic peritoneum, or the uterus itself. How rarely is a pelvic abscess or pyosalpinx found in women who have never been pregnant!

No matter what the opinion held by obstetricians regarding the value of douches in healthy women, all are of the same mind regarding the management of gonorrhœa. All admit that this condition demands active treatment. As a rule, however, the failure to carry out such treatment is supposed to result in a mild form of infection from which the patient may be expected, in the great majority of cases, to recover in a few days. The presence of the gonorrhœal condition is usually inferred from the presence of an acute vaginitis or vulvovaginitis, with redness and perhaps swelling of the vaginal walls or vulva, accompanied by a profuse creamy, greenish-yellow discharge. In the absence of such vaginitis, signs of urethritis are looked for.

The gonococcus is a much more frequent inhabitant of the vagina than such a diagnosis would lead one to believe. In a series of examinations<sup>1</sup> made by me of the vaginal discharge of 113 women, the gonococcus was isolated fifty-two times. These cases represent the average class of women applying for treatment for pelvic disease at hospital clinics. This group of cases consisted of 13 of acute vaginitis, from 8 of which the gonococcus was isolated; 36 subacute cases showed the gonococcus in 22; from 44 cases suffering from chronic pelvic disturbances of one kind or another the gonococcus was isolated twenty-two times; 20 cases showing no evidence of inflammation, examined as controls, showed no gonococcus. The results of this series of examinations show that the gonococcus is a common factor in the production of pelvic disease. More important, however, these experiments prove that it is possible by means

<sup>1</sup> A Contribution to the Bacteriology of the Female Genital Tract, Jour. Med. Research, 1908, xviii, 291.

of a careful technique to demonstrate this organism in the majority of cases in which it is present.

The method of isolation employed in the above series of cases, as well as the cases reported in this paper, is simple. The material to be examined is procured upon a sterile swab, such as is used in ordinary routine bacteriological examinations. The cervix is exposed by means of a bi-valve speculum. After thoroughly sterilizing the external genitals the cervix is cleansed with a series of sterile cotton sponges. The point of the swab is then passed through the os and thoroughly rubbed over the endometrium. A tube resembling that used by Döderlein has been used in a number of cases. This



FIG. 1.—Showing the isolating of colonies of the gonococcus by the stroke methods on blood agar plates.

tube has shown itself to be inadequate as a means of obtaining material, as it only procures the most fluid part of the discharge which is well known to contain the bactericidal properties in largest proportions. The result has been that although numerous organisms are usually seen in the smears prepared from the fresh material, rarely is any growth effected. Within as short time as possible the material on the swab is surface seeded over blood agar. With some experience isolated colonies may be readily procured by this method. As a rule, within twenty-four to forty-eight hours, gonococci, if present, will appear as small, bluish-gray, semi-transparent colonies from 0.5 to 1.5 mm. in diameter (Fig. 1). The observer accustomed to the growth of the gonococcus and other organisms resembling

it will rarely be in doubt as to the nature of the bacteria when a typical growth is produced on blood agar. The results of a very complete test of the relative value of cultural methods of identification, and stained smears of fresh discharges in the above-mentioned series, show that the fresh-stained smear preparation is of little value. In the examination of uterine lochia, the fresh smear is of more help. Here also, however, no definite diagnosis can be made without cultivation of the organisms. The same features which render the examination of the fresh lochia from the uterus of more value than that of the vaginal discharge in general, that is, the larger number of gonococci usually present and the smaller number of contaminating organisms, renders the isolation in cultures correspondingly more easy.

During the past year I have had the opportunity of examining the lochia from 14 cases of severe endometritis following abortion or full-term labor. In all cases the women suffered from definite constitutional disturbances. In all the temperature rose to above 103°. Three patients died and came to autopsy; 2 others developed metastatic pyogenic processes. In addition to the 14 cases examined during life, the bacteriological factor has been determined in 6 other cases coming to autopsy. Of the 20 cases, 4 followed abortion; the other 16 were in women delivered at full term.

The organisms isolated were as follows: Streptococci, ten times in 7 fatal cases; pneumococci, twice in 1 fatal case; *Bacillus aërogenes capsulatus*, 1 fatal case; gonococci five times, and 1<sup>2</sup> four times along with the streptococcus; *Bacillus coli* once in almost pure culture; *Bacillus coli* was also found in larger or smaller numbers in practically every case. Staphylococci, both aureus and albus, were found in large numbers, and saprophytic organisms were frequently found.

In addition to the six pathogenic organisms, a Gram-negative coccus, not resembling the gonococcus either morphologically or in culture, was isolated twice.

In a certain number of cases no growth was procured. This was probably due, in a few cases, to the antiseptic douches which the patients were receiving. Four negative results were undoubtedly due to the use of a tube in the collecting of the material for examination. One of the cases which gave no growth was probably due to the gonococcus.

In my series of 20 cases there are 5 from which the gonococcus was isolated, and 1 in which it was almost certainly present. Only 1 of the cases infected with the gonococcus was fatal. Death was apparently due in this case to a secondary streptococcal infection. All patients, however, suffered from high fever and rapid pulse; 5 had chills. The onset of fever in these cases was early with the

\* See Case II.

exception of 1 case following abortion (Case III); 2 cases (I and V) had a fever of  $102^{\circ}$  before removal from the confinement table. In 1 case (Case VI) the temperature rose to  $102^{\circ}$  on the second day following delivery; it returned to normal the next day, reaching  $104^{\circ}$  again on the eighth day. The remaining 2 cases developed fever on the second and fourth days respectively.

As is usual with all forms of puerperal infection the patients did not realize the severity of their condition. As a rule, they claimed to feel well and protested against being kept in bed. Fever lasted as a rule from one to two weeks. All patients with the exception of one (Case IV), who died, recovered strength comparatively rapidly once free from fever.

Two cases had a profuse creamy, yellow, purulent discharge. In 2 cases (Cases III and IV) the discharge was moderate or scant in amount and mucopurulent in character. Cases I and II presented the false membrane covering the vaginal walls usually associated with a streptococcic infection.

It has been found in the examination of vaginal discharges of acute vaginitis, that other pyogenic cocci such as streptococcus and pneumococcus are not infrequently present in large numbers; sometimes in such large numbers that they seem to be the only organism demonstrable. The history, subsequent examinations, or course of the disease shows in nearly all cases that the gonococcus of Neisser is the primary pathogenic factor. That a similar combination of the gonococcus with one or more pyogenic bacteria in the endometritis following childbirth occurs, certain of the following cases will prove:

CASE I.—Mrs. C. G., primipara. Bacteriological number 07.799. The patient was admitted to the Montreal General Hospital, service of Dr. Lockhart. She had been confined four days previously and was suffering from a bloody, mucopurulent discharge; her fever was high,  $103.4^{\circ}$ ; her pulse, 120 (Fig. 2). The vaginal walls and vulva were covered with false membrane with numerous underlying areas of excoriation. During the last six months of pregnancy the patient had suffered from a profuse greenish, creamy discharge, with redness of the vaginal outlet and excoriations. She had been treated with douches of creolin and mercury bichloride. Before the patient was returned to bed after delivery her temperature had risen to  $102^{\circ}$ , and her pulse was very rapid. The discharge and the severity of her symptoms increased until her entry into the hospital. She was put under constitutional treatment and frequent douches, and left the hospital well on the twenty-fifth day. A smear stained by Gram's method by the doctor in charge one day postpartum contained gonococcoid organisms. A bacteriological examination of the lochia on the day after admission showed *Streptococcus pyogenes* present in large numbers together with a mixture of various Gram-positive and negative bacilli.

In this case, although the gonococcus was never culturally isolated, it appears justifiable in the light of the persisting acute vaginitis, apparently gonorrhœal, and the result of the smear diagnosis of the physician in charge of the case, to classify it as undoubtedly gonorrhœal in origin. At the time, however, of the patient's entry to the hospital she presented the picture of a phlegmonous vaginitis usually associated with infection by *Streptococcus pyogenes*. That this organism was really the cause of the severity of the patient's symptoms, the bacteriological examination proved.

CASE II.—Mrs. J. G., aged thirty-two years, primipara. Bacteriological number 07.729. The patient, three days postpartum had a chill and developed a high fever (Fig. 3) and rapid pulse with more or less profuse bloody, slightly foul-smelling discharge. Upon the

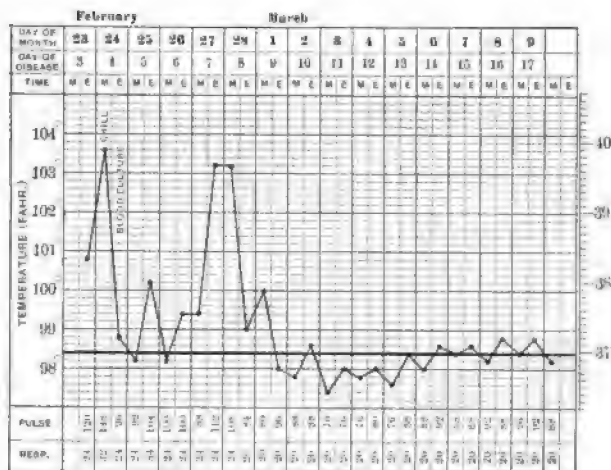


FIG. 2.—Chart of Case I.

fifth day postpartum she was brought to the hospital. When examined on the sixth day the whole vagina was covered with a false membrane of a foul-smelling, sloughy material. Previous to delivery there had been no evidence of any inflammatory disturbance. Delivery had been instrumental and difficult. The strictest technique had, however, been employed. Smears taken from the cervix on the second day after the chill, stained by Gram's method, showed numerous pus cells together with an enormous number of all sorts of organisms including large and small bacilli, many cocci retaining the Gram stain, and a few biscuit-shaped Gram-negative diplococci. Planted upon blood agar, a mixed growth of *Staphylococcus albus* and gonococcoid organisms, as well as several saprophytic organisms, resulted.

This case has been included in the series, although the large

number of contaminating organisms made a diagnosis of the gonococcus impossible.

CASE III.—Mrs. A. P., aged thirty-five years, multipara. Bacteriological number 07.686. The patient was admitted to the hospital

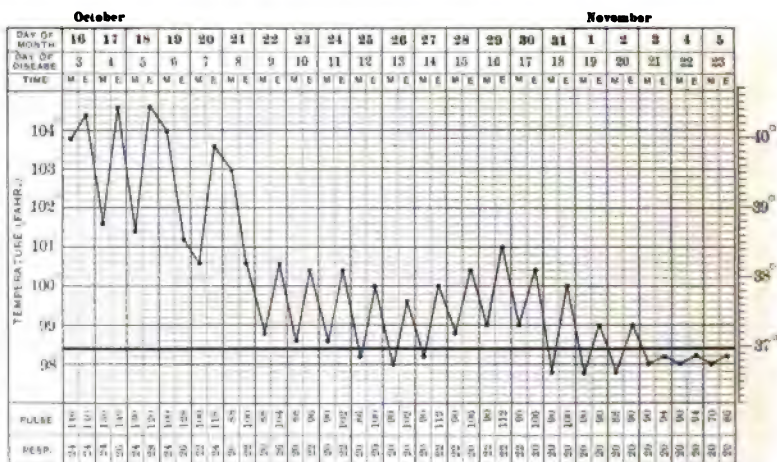
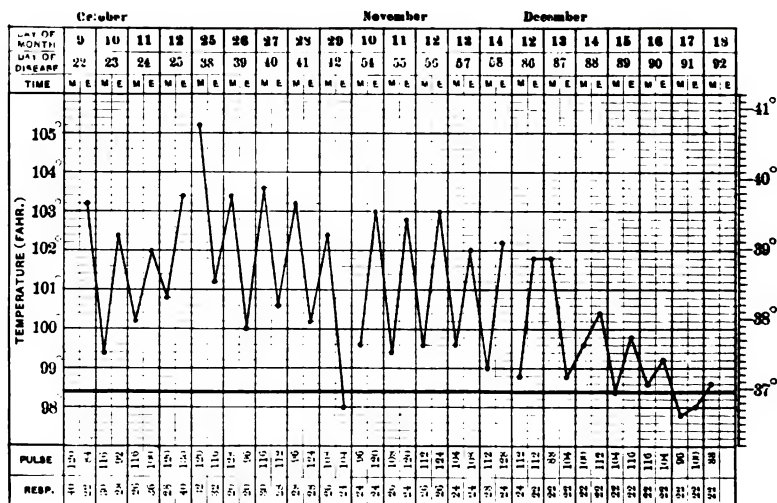


FIG. 3.—Chart of Case II.



arthritis. Three weeks prior to admission the patient had aborted, giving birth to a four months' foetus. She had remained in bed two days following the miscarriage. She continued to lose blood for over two weeks, when she developed a fever and a feeling of malaise. She was curetted, but her condition did not improve. She had had four full-term children, the youngest being ten years old. Up to the present abortion she had had but scant leucorrhœal discharge and no other symptoms of pelvic disturbance.

Bacteriological examination of the uterine discharge, one day after admission, showed numerous pus, few epithelial cells. Many Gram-negative cocci were seen occurring in pairs both inside and outside cells. Numerous chains of cocci (six to ten) retaining the Gram stain, were also seen. Planted on blood agar, in twenty-four hours there was a profuse, raised, semi-transparent growth of grayish colonies, measuring from 0.5 to 1.5 mm. in diameter. Stained by Gram's method these colonies showed Gram-negative, bean-shaped diplococci in pairs and fours. A very few colonies of fine dark points made up of Gram-positive cocci in chains were also seen. Blood cultures taken upon two occasions were sterile. Pus from several metastatic joint conditions and abscesses showed streptococci in pure culture, with absolutely no evidence of gonococci.

This case exemplifies two characteristics of gonorrhœal infection. In addition to the fact that an undoubted gonorrhœal endometritis was followed by streptococcic infection of the uterus which ultimately became general, this case demonstrates the chronicity of gonorrhœal lesions and the freedom from discomfort which the patient often enjoys. In all probability the ten years' period of sterility immediately preceding her last pregnancy had been due to what is by some considered to be the conservative salpingitis which protects women suffering from gonorrhœal infection from the dangers of childbirth and pregnancy. This protection in some way being overcome, pregnancy ensued only to be followed by abortion and an almost fatal termination.

CASE IV.—Mrs. L. T., widow, aged twenty-nine years. Bacteriological number 07.955. Autopsy number 08.14. The patient was admitted to the hospital, service of Dr. F. A. L. Lockhart, December 27, 1907. She had aborted at three and one-half months two days before, since when she had considerable bleeding. Before admission her temperature was 100° and her pulse 112. Six hours later these were: temperature, 104°; pulse, 30 (Fig. 5). The uterus was cleansed with the finger and lightly with a sharp curette, and douched with sterile saline solution. A large piece of foul-smelling chorionic tissue was removed. Microscopically this tissue showed numerous polymorphonuclear leukocytes. From December 28 to January 9 the patient's temperature was septic in type, and during this time she suffered from chills of more or less marked severity. She complained of but little distress always

replying when asked regarding her condition, "je me porte mieux." She suffered from very rapid respirations and at one time had a sharp attack of dyspnoea with cyanosis and gasping. On January 9, 1908, a mass was palpable to the left of the uterus. A vaginal incision was made under spinal anesthesia and a small quantity of pus evacuated. An abdominal incision was made and the left ovary, which was filled with pus, was removed. The patient's condition, however, did not improve and she died January 10, 1908. Two examinations were made of the uterine discharge. (B. 07.955.) Stained by Gram's method the fresh pus shows numerous pus, few epithelial cells. A small number of Gram-positive cocci were

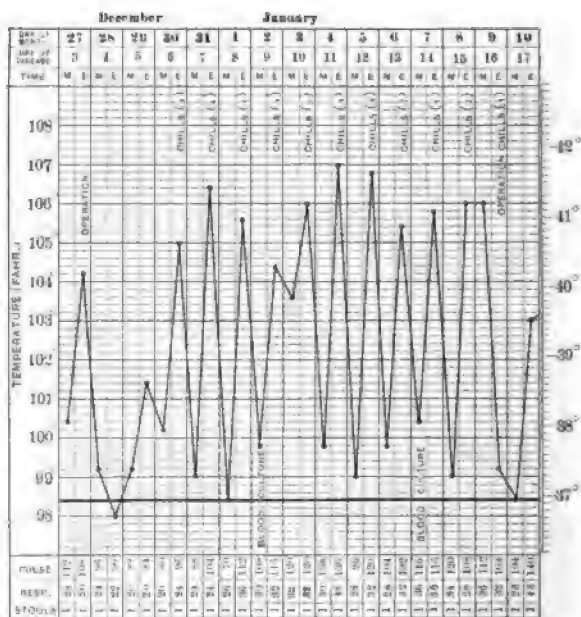


FIG. 5.—Chart of Case IV.

seen, mainly in pairs. There were numerous Gram-negative bacilli with rounded ends, for the most part occurring singly. Moderate numbers of diplococci gonococcoid in shape, decolorizing by Gram's method were seen both inside and outside cells. Planted upon blood agar, no growth occurred at the end of forty-eight hours. The failure to obtain a growth was undoubtedly due to the antiseptics used in the douches.

Second examination (B. 08.8): Stained by Gram's method the fresh pus showed large numbers of pus cells. Numerous Gram-positive cocci in pairs and chains of four were seen. Many Gram-positive and negative bacilli were found. There were also a few



pairs of well-formed, biscuit-shaped, Gram-negative cocci. Planted upon blood agar, in twenty-four hours the surface was moderately covered with isolated colonies of *Bacillus coli*; fine colonies of Gram-positive cocci in pairs; and two fine, grayish, semi-transparent colonies, 1 mm. in diameter, of gonococci. During the course of the disease blood cultures were attempted upon two occasions, but proved negative. Autopsy was performed sixteen hours after death. The anatomical diagnosis was: Acute diffuse peritonitis; puerperal septicemia (streptococcus); acute gangrenous endometritis; multiple abscesses of uterus; phlebitis with thrombosis of peri-uterine veins; multiple pelvic abscesses; acute vaginitis; acute suppurative oöphoritis; acute suppurative nephritis; oedema of the lungs; fatty liver; healed gummas of the liver; chronic pul-

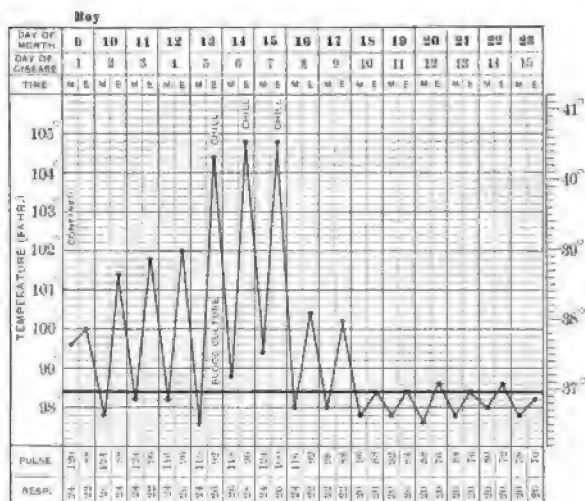


FIG. 6.—Chart of Case V.

monary tuberculosis; chronic pleuritis; chronic pericarditis; acute splenitis; congestion of the liver and kidneys; laparotomy; salpingectomy; vesesection; vaginal section.

CASE V.—Mrs. D. D., aged thirty-two years. Bacteriological number 07.289. The patient was delivered in the Montreal Maternity Hospital of a full-term child. Labor was normal. From the time of delivery the patient suffered from a fever of 100° or more. On the fifth day postpartum she had a chill and the temperature rose to 104.2° (Fig. 6). She complained of little pain and no distress. The uterus involuted well, although a profuse, creamy, greenish-yellow discharge developed. No interference was attempted with the exception of one intra-uterine douche and repeated vaginal douches. The patient left the hospital apparently well. The child, however,

developed a severe ophthalmia neonatorum which led eventually to septicemia and death. On questioning the husband it was found that he was being treated for kidney disease. This was found, on examination, to be a case of frank, acute, gonorrhoeal urethritis. Smear shows numerous pus, few epithelial cells. Many bean-shaped Gram-negative diplococci were seen. These were situated both inside and outside the pus cells. Many cells presented a "typical" appearance, being filled with closely packed gonococoid organisms. Planted upon blood agar, in forty-eight hours, a moderately profuse almost pure growth of gonococci developed. A similar organism was also isolated from the baby's eyes.

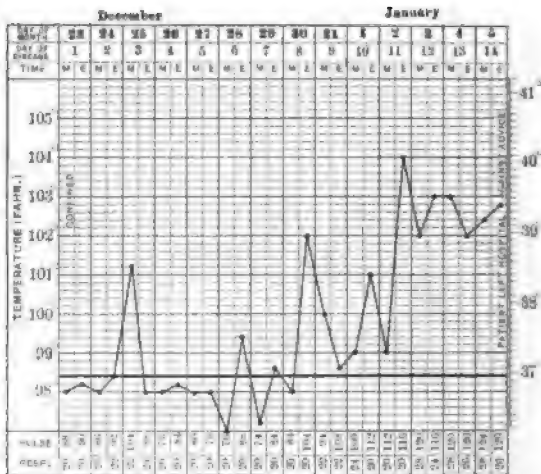


FIG. 7.—Chart of Case VI.

CASE VI.—Mrs. S., aged twenty-six years. The patient was confined in the Montreal Maternity Hospital. Labor was normal. Two days after delivery the patient's temperature rose to 101.1°. It fell to normal the next day, but rose to 102° upon the eighth day; two days later it rose to 104° (Fig. 7). The patient's temperature remained up and she left the hospital, against the advice of the physician in attendance, on the fourteenth day postpartum. The lochia consisted of a profuse, creamy, greenish, purulent discharge which persisted at the time she left the hospital. The child showed no signs of ophthalmia. No history was obtained of any antepartum inflammatory condition.

The smears showed numerous pus, few epithelial cells. Many Gram-negative bacteria with rounded ends were seen, also Gram-positive cocci in pairs. One or two pairs of Gram-negative bean-shaped diplococci were also found. In twenty-four hours a culture upon blood agar showed several large, isolated, greyish, creamy colonies of *Bacillus coli*; also a few white colonies of *Staphylococcus*

albus. Between these larger colonies numerous small, semi-transparent colonies of gonococci were seen.

CASES V and VI demonstrate the severity of the disease which an uncomplicated gonorrhoeal infection may produce. The unfortunate ending, too, of the ophthalmia in the child from Case V also brings before us the importance of the gonococcus in the pregnant and puerperal woman.

Although Case II was probably gonorrhoeal, I will, for the purpose of this paper, speak only of the other 5 cases. In all of these the infective process began as a gonorrhoeal condition. In all the most careful technique had been followed during delivery. Nevertheless 5 patients became septic and ultimately suffered from severe infection. In 3 this infection was undoubtedly due to streptococci.

All physicians dealing with large numbers of pregnant women have seen cases in which fever, at times severe, has followed spontaneous or precipitate labor, in which absolutely no examination of the internal parts had been made. Experience shows, also, that it is in unmarried girls that fever is most frequently met with. It is naturally in women illegitimately pregnant that gonorrhoea is most frequently found. Cases such as these influence Lenhartz and others to support the prophylactic douche. Many cases occur in which retained secundines, filth of the external parts, and other causes are insufficient to explain the development of the infective process.

In 1898 Burr, in an article entitled "Gonorrhoea as a Factor in Puerperal Fever," puts the question which he proceeds to answer: "Notwithstanding advancement along the lines of antiseptics, etc. . . . why is there not greater freedom from septic puerperal infection?" He draws attention to the prevalence and chronicity of gonorrhoea and states the idea, which I have expressed above, in the following words: "The gonococcus will share its possessions in apparent harmony with other pathogenic germs, or at an indefinite period quit the field in their favor."

My own experience, as well as those of many observers, seem to prove that streptococci are rarely found in the upper part of the vagina. The streptococcus, as well as numerous other organisms, is, however, undoubtedly present in the lower part of the vagina and about the vulva. Thus different investigators have had different results owing to different technique. Williams is probably correct when he says "that in those cases (in which pathogenic organisms are found in the upper vagina) the infection is probably carried up by the instrument made use of in procuring material for examination."

Other opinions and clinical experiences, on the contrary, are due, I believe, to the fact that sufficient account has not been taken

of the likelihood of auto-infection occurring in cases of chronic gonorrhoea.

CONCLUSIONS. (1) The gonococcus either alone or as a primary infecting agent plays a much more important role in the production of puerperal fever than is usually appreciated by most observers; (2) various microorganisms especially the streptococcus and *Bacillus coli* are usually present about the vaginal outlet, although apparently infrequently found in the upper part of the vagina of the healthy woman. These organisms are ever ready to attack the tissue whose resistance has been destroyed by the action of the gonococcus. As corollaries there follow (a) the necessity for the most careful examination of the history of the patient and of the vaginal discharge early in pregnancy in all cases presenting the least grounds for suspicion; (b) the necessity for more than ordinary caution in examining externally all pregnant women presenting even the slightest evidence of an inflammatory condition.

I wish to express my thanks to Dr. F. A. L. Lockhart for use of cases in the Montreal General Hospital, as well as the physicians of the Montreal Maternity Hospital for notes upon cases in that institution. I wish also to thank Dr. C. W. Duval for numerous suggestions from time to time.

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## A NEW METHOD OF STAINING THE DIPHTHERIA BACILLUS.

BY WM. H. RUSH, A.M., M.D.,

OF ST. LOUIS, MO.

THE following are the materials required in a new staining procedure: Grüber's methylene blue; Grüber's eosin, "W. G.," or "rein;" tartaric acid; alcohol, 96 per cent.; and distilled water.

The solutions should be prepared as follows:

(a) Saturated aqueous solution of methylene blue, filtered, 10 c.c.; tartaric acid, 10 per cent. aqueous solution, 10 c.c.; distilled water, 80 c.c.

(b) Tartaric acid, 10 per cent. aqueous solution, 10 c.c.; alcohol, 96 per cent., 50 c.c.; distilled water, 40 c.c.

(c) Eosin, saturated aqueous solution, filtered, 1 c.c.; distilled water, 199 c.c.

Stain thin films—on a coverglass or slide, fixed by the flame in the usual way—ten seconds in *a*; wash ten seconds in *b*; stain ten seconds in *c*; blot and dry. The solutions *b* and *c* should be poured on freely. Drying or washing in water between the different steps is unnecessary.

The polar bodies will be stained deep violet-blue; the remainder

1



2



3



4



5



FIG. 1. Two hours' culture; a combination of portions of two fields.

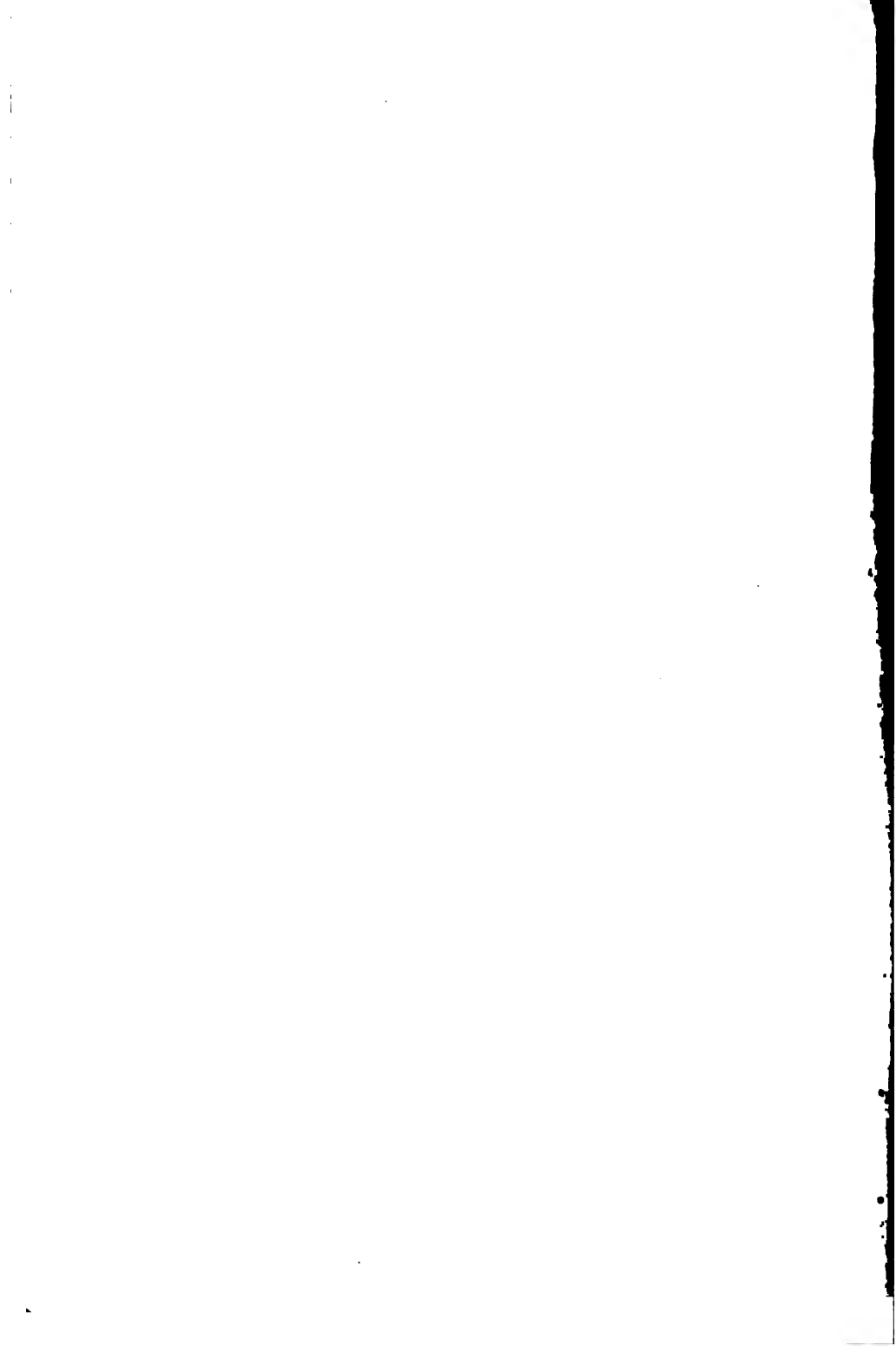
FIG. 2. Fourteen hours' culture.

FIG. 3. Twenty-one and one-fourth hours' culture.

FIG. 4. Ten days' culture.

FIG. 5.—Smear direct from nasal discharge.

The figures were drawn with camera lucida, Zeiss  $\text{Y}_2^1$  --4.



of the bacillus and all other microorganisms that I have observed, with the exceptions mentioned below, intense pink (Figs. 1, 2, 3, 4, and 5). Tissue elements, fibrin, mucus, etc., in case of films direct from the throat or nose, also are stained pink.

I have tried all the easily obtainable organic acids, as well as propionic and butyric, with the above stains, in a great variety of proportions and combinations, and have fixed upon the method described as the most suitable. Butyric acid, substituted for tartaric in solution *a*, and used in simple 1 per cent. aqueous solution in place of *b*, gives somewhat better results than tartaric acid as in the above formula. But the disgusting odor of butyric acid renders its use impossible, except in isolated laboratories.

The method has wide working limits, both as to the composition of the different solutions and as to the timing of the different steps in the process of staining. Solution *c*, however, must not be used too long or too strong.

I have tried this method many times, have controlled it by the stains of Löffler, Neisser, and Hunt, and have confidence in its reliability. I have successfully stained the bacillus from cultures of all ages between the limits of two hours and ten days. The appearance of the bacillus may be best comprehended by reference to the accompanying illustrations.

*Staining Properties of Other Bacteria.* Many cocci, of various habits of growth, occasionally show a more or less distinct blue central portion. The strong contrast-stain easily reveals their true morphological character. I have found a few species of leptothrix which show metachromatic granules with this stain and with Löffler's, but not with Neisser's stain. The relatively small granules and the coarse filaments or segments ought to make confusion of this form with the bacillus of diphtheria impossible.

*Bacillus Pyocyaneus.* I was furnished a pure culture of this organism by Dr. Simon, of the City Bacteriologist's Laboratory, who isolated it from a case of gangrenous appendicitis. Companion smears of this culture, stained by the method herein presented, and by the methods of Löffler and Neisser, all show here and there a bacillus with one or two metachromatic granules, precisely resembling a diphtheria bacillus of the short variety. The same is true, as pointed out to me by Dr. Simon, of smears stained with thionin blue. Its occurrence and mode of growth exclude the possibility of a mistake in diagnosis.

*Pseudo Bacillus.* I have examined a number of strains of this group of organisms, sent me in pure culture by Dr. Alice Hamilton, of the Memorial Institute of Chicago. They stain as follows:

1. Obtained from the throat of a diphtheria convalescent. A few bacilli show metachromatic granules, when stained by the method of Neisser, also with methylene blue and eosin according to the above formula; none, however, with the butyric acid modification.

2 and 3. Scarlatinal otitis media. No metachromatic granules by any method used.

4. Scarlatinal otitis media. A few bacilli show metachromatic granules with Neisser's stain and with methylene blue and eosin.

5. Chronic otitis media. A few metachromatic granules with Neisser's stain, none with methylene blue and eosin.

6. Postscarlatinal otitis media. A few metachromatic granules with Neisser's stain and with methylene blue and eosin.

*Staining of Smears Direct from the Throat or Nasal Discharge.* In the examination of 20 cases, 13 positive, 7 negative, my findings agreed with those obtained from the corresponding cultures. In one case which I reported as doubtful, the first culture showed no bacilli at eighteen hours' incubation. A second culture, obtained fifteen hours later, showed a very few diphtheria bacilli after twenty-four hours' growth. I do not, however, advocate reliance upon the direct examination, except in positive cases.

The advantages of the suggested staining method are: Accessibility of the necessary reagents; ease of preparing the staining solutions; wide working limits; and striking and characteristic appearance of the organisms when so stained.

## THE NATURE OF POSTOPERATIVE FEMORAL PHLEBITIS.

BY WALTER HERMAN BUHLIG, B.S., M.D.,

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In looking up the subject of postoperative phlebitis, I have been impressed with the lack of definite classification of the different cases. The fact is that in most of the current literature and in most text-books the terms phlegmasia alba dolens, thrombophlebitis, phlebitis, and thrombosis, relating to the femoral vein, are used synonymously. One author<sup>1</sup> says that when phlebitis is in the femoral or iliac veins the disease is known as phlegmasia alba dolens. Another author<sup>2</sup> states that thrombosis of the femoral veins is the same as that described in text-books under the name of phlegmasia alba dolens. Kaufman<sup>3</sup> says that phlegmasia alba dolens is a thrombophlebitis retrograde from the iliac to the femoral vein.

It is doubtful whether these definitions are quite accurate, and it is my purpose to show that sufficient differentiation has not been made in the description of the postoperative complications grouped under the headings of phlebitis, thrombosis, and thrombo-

<sup>1</sup> International Text-book of Surgery, 1899, vol. i, p. 892.

<sup>2</sup> Johnson, Surg., Gyn., and Obst., iii, p. 111.

<sup>3</sup> Specielle Pathologie, p. 93, 4th edition.



phlebitis. I expect to prove (1) that many of the cases are really nothing but phlegmasia alba dolens in its proper sense; (2) that in this condition thrombosis is not necessarily present; and (3) that therefore many of the cases are not correctly described.

Pathologically there are three primary conditions: (1) Phlegmasia alba dolens; (2) thrombosis; (3) phlebitis. In addition, there may be secondary phlebitis (thrombophlebitis) from an infected thrombus, and also a phlegmasia in the same manner. Further, thrombosis of some degree may follow an initial phlebitis, and primary phlegmasia alba dolens may lead, through phlebitis, to thrombosis.

Phlegmasia alba dolens is a term very loosely used, and, unless one desires to convert its meaning, should be applied to those cases in which there is an acute swelling of the connective tissue of the thigh due to a descension of a pelvic cellulitis<sup>4</sup> involving first, and often exclusively,<sup>5</sup> the upper part of the thigh. This swelling leads to compression of the veins and sometimes secondarily to thrombosis, but it is a misuse of the term phlegmasia alba dolens to call by this name all primary thrombi in the thigh. Besides Olshausen, Schroeder<sup>6</sup> and v. Winckel<sup>7</sup> are in unison on this point. Virchow<sup>8</sup> in 1862, discussing parametritis, showed that what some had called phlebitis is really a lymph thrombosis, making it all the more improper to discuss phlegmasia alba dolens as primary bloodvessel thrombi. It is just as incorrect, likewise, to speak of thrombosis, phlebitis, and the like when the condition is that of lymphatic involvement only, even though the former conditions become sequels. As mentioned, phlegmasia alba dolens makes œdema first in the thigh and may descend, but not necessarily, whereas primary femoral thrombi produce œdema first in the foot or calf.

To obtain data for my contention, I have read most of the literature relating to the so-called phlebitis after operation. To add here the titles of the articles would be mere repetition, for they are already summarized in some recent literature. (See Morley,<sup>9</sup> Grant.<sup>10</sup>) It is only just to state that in the description of many of these complications specific mention is made of the actual conditions that obtained, and many cases are properly classified; but in a goodly number of histories of cases the statement is made only that the leg is swollen, without distinction as to calf or thigh and without specification of the place where the swelling or edema began, making, for my purpose, some indecision. But some cases, from their description (see Morley, Cases IX and X), and some from their rapid convalescence, can be nothing but phlegmasia alba dolens, and are classed under

<sup>4</sup> De Lee, Notes on Obstetrics, 1904.

<sup>5</sup> Olshausen-Veit, Geburtshilfe, 1902, p. 778.

<sup>6</sup> Geburtshilfe, 4th edition, 1874, p. 716.

<sup>7</sup> Lehrbuch der Geburtshilfe, 2d edition, p. 779.

<sup>8</sup> Virchow's Archiv, xxiii, p. 415.

<sup>9</sup> Surg., Gyn., and Obst., September, 1907.

<sup>10</sup> Jour. Amer. Med. Assoc., xlviii, p. 567

other headings. Even in those cases in which a thrombus is reported as having been felt it is possible that a compressed vein was found.

Concerning the accuracy of the use of the term phlebitis to describe these postoperative conditions, it seems to me that it cannot be correctly employed. As I understand phlebitis, it alone can never be considered when there is swelling of the leg, for then there must be present either thrombosis or phlegmasia alba dolens also, or both. If that is correct, practically all of the cases reported under that heading are improperly classed, for I believe that all these postoperative complications that have been reported have had associated with them some swelling.

Aside from this latter consideration, which I advance without any spirit of quibbling, the question really at issue is not whether thrombosis ever accompanies, or is the result of, phlegmasia alba dolens. That is a fact and cannot be gainsaid. The point in controversy is that some cases of phlegmasia alba dolens run their course without any thrombotic process whatever, and it is therefore imperative to class these by themselves for the sake of accuracy, if for no other reason.

Concerning the literature upon this point, it appears all to be old, and I can find very little. There are numerous references (Olshausen-Veit, von Winckel), but in practically all the articles that are at my disposal the association of thrombosis and phlegmasia is noted.<sup>11</sup> These are findings at autopsy. Since phlegmasia alba dolens is due to an infection, it would be only natural to find thrombosis in the patients that die, for in the more virulent infections, it is acknowledged the process may lead to thrombosis. Upon the point whether phlegmasia alba dolens ever is found without thrombosis, the affirmative statement of Olshausen, v. Winckel, and Schroeder may be mentioned. Schmaus<sup>12</sup> states that phlegmasia alba dolens is a phlegmon without preceding thrombus. Lee's finding,<sup>13</sup> that a marked phlebitis may exist without thrombosis, is to the point, as is also, more convincingly, the evidence of Klob.<sup>14</sup> This author states that he has seen cases with excessive oedema of the lower extremity without coagulation in the veins, and really answers our question by affirming that thrombosis of the veins is not always associated with phlegmasia alba dolens.

Making a conclusion from these considerations, it is my judgment that the term phlebitis cannot be used correctly in this connection. Further, that though many of the cases are properly described as thrombosis or thrombophlebitis, many, on the other hand, must be designated phlegmasia alba dolens because of the pathological nature of this condition and because of the similar conditions that obtained in the particular cases in question.

<sup>11</sup> Davis, also Mackenzie, quoted by Harvard, *Lancet*, 1906, i, p. 645; also Pourtales, *Archiv f. Gynäkologie*, lviii, p. 36.

<sup>12</sup> *Grundriss der path. Anat.*, 6th edition, p. 699.

<sup>13</sup> Quoted by v. Winckel, *loc. cit.*

<sup>14</sup> *Path. Anat. of Female Sexual Organs*, Translation, 1868, p. 288.

## REVIEWS.

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**THE DISEASES OF CHILDREN.** Edited by M. PFAUNDLER, M.D., Professor of Diseases of Children in the University of Munich; and A. SCHLOSSMANN, M.D., Professor of Diseases of Children in the Medical Academy of Düsseldorf, Germany. English translation, edited by HENRY L. K. SHAW, M.D., Clinical Professor of Diseases of Children in the Albany Medical College; and LINNÆUS LAFETRA, M.D., Instructor in Diseases of Children in Columbia University, New York. Four volumes. Vol. I, pp. 440; Vol. II, pp. 619; Vol. III, pp. 552; Vol. IV, pp. 543. 61 full-page plates, and 430 text cuts. Philadelphia and London: J. B. Lippincott Co., 1908.

PFAUNDLER and SCHLOSSMANN's *Diseases of Children* is in many respects a monumental work which, having achieved an enviable repute in Germany, has now been made available to the large number of English-speaking physicians unacquainted with German. The contributors number about fifty; all are very well qualified to speak on the subjects that they discuss; some are already well known beyond the confines of their native land. Volume I comprises a discussion of the general pathogenesis and pathology, mortality and morbidity of childhood, and of the symptomatology, prophylaxis, and therapeutics of diseases of children, as well as disorders of nutrition and metabolism; the contributors are Hamburger, Pfaundler, Bendix, Neumann, Prausnitz, Raudnitz, Engel, Camerer, and Sommerfeld. Volume II deals with special diseases of definite ages, general disorders, and infectious diseases, the contributors being Knöpfelmacher, Rommel, Seitz, Japha, Hecker, von Starck, Stölzner, von Noorden, Salge, Moser, von Pirquet, von Bokay, Swoboda, Voigt, Trumpp, Moro, Fischl, Langer, Spiegelberg, Neirath, Ibrahim, Hochsinger, and Schlossmann. Volume III comprises diseases of the digestive, respiratory, and circulatory systems, the contributors being Moro, Finkelstein, Fischl, Pfaundler, Selter, Langer, Stooss, Freund, Schlossmann, Feer, Gallatti, Friedjung, Hochsinger, and Siegert. Volume IV deals with diseases of the urogenital and the nervous systems and diseases of the skin, the contributors being Langstein, Pfister, Zappert, Thiemlich, Galewsky, and Leiner.

The multiplicity of the subjects and the detail in which they are

discussed preclude specific mention of the many meritorious contributions. If one should single out for special commendation the articles on general symptomatology (200 pages) by Pfaundler, general therapeutics (40 pages) by Neumann, scarlatina (53 pages) by von Pirquet and Shick, diphtheria (64 pages) by Trumpp, syphilis (68 pages) by Hochsinger, tuberculosis (45 pages) by Schlossmann, and disorders of nutrition (90 pages) by Fischl, it is done fully conscious of the many other, some shorter, contributions of more than usual merit. Perhaps some of the statements on controversial points will not strike a responsive chord in many readers; others will observe with ill-concealed regret the defects inherent in composite works—disproportionate allotment of space, inequalities in the manner and the method of treating different subjects, overlappings, repetitions, etc. These, however, are nowhere obtrusive, and they are far outweighed by the merits of the work. A noteworthy feature consists of the emphasis placed throughout on the clinical aspects of disease, on the symptomatology, including disturbed physiology, and on diagnosis and treatment—a feature that the general practitioner will prize highly. The editors and the translators have done their work well. The work must be unreservedly commended.

A. K.

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**CANCER OF THE WOMB: ITS SYMPTOMS, DIAGNOSIS, PROGNOSIS, AND TREATMENT.** By FREDERICK J. McCANN, M.D., F.R.C.P., F.R.C.S., Physician to In-Patients, Samaritan Free Hospital for Women, London. Pp. 160; 47 illustrations. London: Henry Frowde, Oxford University Press, and Hodder & Stoughton, 1907.

DR. McCANN has prepared a very interesting book. Without attempting the elaborate presentation of Cullen, he has published a valuable reference volume, which is especially suited to the general medical reader. The book opens with an introductory chapter upon the anatomy of the pelvis and its contained organs, and this is followed by a discussion of the various etiological theories. Particular attention should be called to his statement that we must depend upon better medical education, and not upon the distribution of leaflets among women, in our endeavor to cope with uterine carcinoma. With this view we are only in partial accord, since we believe that it is better that many patients be needlessly alarmed than that ignorance and the folklore relative to the menopause should continue the present slaughter. Chapters upon cancer of the neck and body of the womb, and upon spreading of uterine cancer follow. In the last-mentioned chapter, upon page 43, there

is evidently a typographical error in the statement that "before the abdominal operation becomes the method of choice for operation for cancer of the uterus the mortality must be *not less* than the vaginal method, and the freedom from recurrence greater."

The chapter upon diagnosis is pleasing. Here, as elsewhere, there is a profusion of illustration, as well as the introduction of many of the case histories collected from the author's practice. He is an advocate, we are glad to see, of hysterectomy upon the diagnosis of senile endometritis, quoting Matthew Duncan's statement, that "retrospective diagnosis is not of much value to your patient." A chapter is devoted to the microscopic appearances and diagnosis, and the author then contributes a very satisfactory chapter dealing with the surgical treatment of uterine cancer. Amputation by the galvanocautery, the supravaginal amputation of the cervix (Schroeder), and the abdominal total extirpation of the uterus, as well as the vaginal hysterectomy, are described. As will be seen by study of the contained series of case reports, the author has a decided predilection for the vaginal method, but he gives a full description of his technique of the abdominal operation. In connection with the description of the vaginal method, the incisions of Schuchardt are included. Chapter VIII, upon the value of vaginal total extirpation of the cancerous uterus, is composed of several pages of statistics and an account of the extended abdominal operation by the method of Wertheim. The author is not favorably disposed toward what are designated "dissection operations" (as that advised by Ries, of Chicago), believing that there is no analogy between the breast and the uterus in this matter. He is, however, in favor of the Wertheim procedure, being of the belief that the value of the method is mainly found in the removal of the parametrium and upper vagina. He would, indeed, advocate the removal of the upper half of the vagina in vaginal and abdominal operations for cancer of the cervix. This chapter is one of the best in the book, and we are heartily in accord with his statements, except as regards the vaginal method of attack.

Chapters upon the treatment of inoperable uterine cancer and upon sarcoma of the uterus follow, while the last chapter of the book proper is devoted to a most interesting dissertation upon syncytioma malignum, of which the author has had four cases. Chapter XII is largely devoted to the case histories comprising the author's colated experience. The book closes with a very satisfactory chapter upon the after-treatment of operations for cancer of the womb. While space prevents any detailed consideration of the directions contained, we are constrained to say that it is one of the most sane and advanced expositions of which we have knowledge. W. R. N.

**A SECOND STUDY OF THE STATISTICS OF PULMONARY TUBERCULOSIS: MARITAL INFECTION.** By ERNEST G. POPE, of the Adirondack Cottage Sanitarium, Saranac Lake, New York. Edited and revised by KARL PEARSON, F.R.S. With an appendix on assortative mating from data reduced by ETHEL M. ELDERTON. Pp. 36. London: Dulau & Co., 1908.

It has long been considered a proper thing to begin all statistical articles upon medical subjects with an apology; but without doubt no apology, however abject, is sufficient excuse for many numerical essays foisted upon the medical profession by some of its members. It is a curious fact that while all medical knowledge must, in final analysis, rest upon statistical data, so little attention has been paid to this side of mathematics in our American universities. The result is that not one physician in a thousand can either prepare or understand a paper based upon the most accurate statistical methods now employed. Prof. Karl Pearson, of the University of London, has really founded and developed this branch of medicine. His work upon inheritance in tuberculosis is the best treatment of the subject, and he proves that there is undoubtedly a strong hereditary tendency.

At the time of his death the late Ernest G. Pope, statistician at the Adirondack Cottage Sanitarium, Saranac Lake, was engaged in applying many of these newer mathematical methods to the various problems connected with pulmonary tuberculosis. He left a manuscript nearly completed, dealing with marital infection, which Professor Pearson has completed, enlarged, and published as "A Second Study of the Statistics of Pulmonary Tuberculosis." It has long been taken for granted that the close and prolonged exposure of husband and wife resulted in the infection of the healthy partner in a large number of instances. But the problem is not so simple. Professor Pearson and others have proved, for example, that the inheritance of various physical qualities, as well as this problem, can be dealt with only by a study of the coefficient of correlation, a process involving considerable mathematical knowledge.

Mr. Pope had demonstrated that there is a sensible correlation between the presence of tuberculosis in husband and wife, and that assortative mating plays a very important part. The latter section he had planned to elaborate. Husband and wife, Pearson has found, bear resemblance in regard to eye color and the occurrence of insanity, neither of which can, of course, be assumed to be due to infection. So it is impossible to assume that the resemblance in tuberculosis is due wholly to infection, but, on the other hand, if the tuberculous diathesis be inherited, the parents of tuberculous offspring, who are considered in this paper, must be looked upon as a selected group and corrections applied accordingly. After applying this correction it is seen that the average action of assortative

mating is not sufficient to explain all the resemblance, and that a sensible but not very large effect of infection is present.

The literature has been exhaustively studied, and 41,786 couples have been dealt with. The body of the article is taken up with intricate mathematical formulæ, and the first appendix contains a proof of the fundamental formulæ employed. In the second appendix, Miss Elderton has discussed assortative mating in man in regard to many characteristics, such as health, general intelligence, temper, success of career, insane diathesis, and, finally, in regard to the tuberculous diathesis.

The conclusions of this study are that there is some sensible but slight infection between married couples, that this is largely obscured or forestalled by the fact of infection from outside sources, that the liability to the infection depends on the presence of the necessary diathesis, that assortative mating probably accounts for at least two-thirds, and infective action for not more than one-third of the whole correlation observed in these cases. Professor Pearson calls attention to the fact that to be able to apportion accurately the action of infection, assortative mating, and inheritance, fuller details in regard to the ages of husband and wife at marriage, the ages at the onset and death, as well as the age of the parent at the birth of the child, and the age at onset and death of the child, should all be recorded. Professor Pearson adds that he can only join in the general regret that the medical profession should have lost at such an early age a statistician like Mr. Pope, so capable of throwing light on the numerical aspect of medical problems.

The paper is very valuable. It is to be hoped that in America, as well as in England, an awakening to the value of the application of trustworthy statistical methods to medical subjects will soon be apparent.

L. B.

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DIE ENTZÜNDUNG; EINE MONOGRAPHISCHE SKIZZE AUS DEM GEBIET DER PATHOLOGISCHEN PHYSIOLOGIE. By RUDOLF KLEMENSIEWICZ, Professor of General Pathology in the University of Gratz, Austria. Pp. 120; 2 illustrations. Jena: Gustav Fischer, 1908.

OUTLINING in easy but creditable manner the general process of inflammation in this production, which he modestly describes as a sketch, Professor Klemensiewicz seeks especially to explain in satisfactory manner the basic phenomena of inflammation in the light of modern ideas of physics. His definition of the process runs somewhat as follows: "Inflammation is a process induced by some agency which, in influencing the tissues, coincidentally produces some actual disturbance in the condition of the walls of the blood-vessels, in consequence of which there occur escape of the fluid and

formed elements from the vessels into the surrounding structure and, at the same time, a reaction on the part of the tissue elements still vital in the inflammatory focus. This reaction of the tissue manifests itself partly in biological progressive phenomena, partly in necrobiotic changes." The nature of the alteration of the vascular wall may be of varying grade and varying in its essence, but it is characterized by an increased permeability, in a broad sense is commonly induced by chemical means, is attended by loss of the power of nervous response of the vessel wall and by a consequent paralytic dilatation, by an increase in the circulatory pressure in the area, and by the phenomena of transudation and cellular emigration. Stress is laid upon the phenomenon of a heightened circulatory pressure in the inflamed area, and its experimental demonstration, although a satisfactory explanation of its cause is not given. Such a factor existing, however, the author sees therein a potent element in the explanation of the peripheral accumulation of the leukocytes in the blood stream, the transudation of the fluid, the escape of the white cells, and exceptionally of the red corpuscles. To him it is the moving pressure of the column of heavy red cells which forces from their midst more and more the lighter elements, and mainly determines their passage through the vascular wall, for diapedesis only occurs when the column of blood is circulating, not when, even under pressure, it is stagnant and its elements all mingled in a confused mass. Were the chemotactic theory, or that of cellular motility the real explanation, diapedesis would prevail as well in the latter stage as when there is forceful movement of the blood column. While, thus, the author appeals freely to the idea of filtration under pressure for the phenomena of transudation, he unhesitatingly adverts to the idea of osmosis and diffusion and to tissue contribution for the explanation of the quality of the transudate as found. A considerable part of the pamphlet is devoted to a careful consideration of the theories of lymph production as basic to an understanding of the phenomena of inflammatory transudation, leading to acceptance mainly of the combination of the features just indicated. By detailed physical methods, based upon the ideas of Körner and his followers, the author demonstrates how the increased force of circulation within the vessels of the inflamed area lead through the accumulation of the transudate and other extravascular pressure factors upon the venous side of the capillary system to compression of the vessels and hindrance of flow, eventuating in the succeeding stasis as a later stage. These physical demonstrations are particularly illuminating and satisfactory, and doubtless, employed in logical and discreet connection with the factors of other well-known explanations, should be credited. The application of similar ideas to explain the predominant part the bloodvessels play in resorption of transudate follows in easy sequence, the author's views as to "back filtration" being marked particularly by the indication



of the venous side of the capillary area and venules as the seat of the process, and the necessity for especial structural relations between the vessel wall and the surrounding tissue, as well as the existence of a proper difference between the intravenous and the tissue-fluid pressure for its proper procedure.

There are numerous interesting details which one concerned in the precise study of inflammation will follow with interest, but which here cannot be pursued for want of space; there are minor factors which might fairly be criticised, and one wishes for a wider discussion of the fundamental factor of active circulatory pressure and its explanation; but, aside from these, the brochure must be acknowledged an extremely interesting and luminous exposition and one sure to command the attention and respect of students of pathology.

A. J. S.

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DISEASES OF THE SPINAL CORD. By R. T. WILLIAMSON, M.D. (London), F.R.C.P., Assistant Physician of the Royal Infirmary and Lecturer in Medicine in the Victoria University, Manchester, England. Pp. 432; 183 illustrations and 7 plates. London: Henry Frowde, Oxford University Press, and Hodder & Stoughton, 1908.

It is evident that the author of this book had in mind the needs of the medical student. For clearness of diction and excellence of style there are few books which come up to the standard set by this work, and it is, indeed, a pleasure to commend it. It is by no means an exhaustive presentation of spinal cord diseases, but from the very beginning the author presents the cardinal facts sufficiently to make it quite enough for the medical student and the practitioner. It is also one of the few books in which the illustrations are not borrowed, for with one exception every one is original, and there are altogether 183 illustrations and 7 plates. It may also be added, in passing, that the illustrations are unusually good, and, what is more important, they are lucidly explained by their titles.

In the beginning of the book the structure of the spinal cord is taken up, and this is followed by general pathological histology, degeneration of nerve fiber tracts and cells, functions of the spinal cord, symptoms of spinal diseases, with an account of electrical and x-ray examination and lumbar puncture. The diagnosis and localization of diseases of the spinal cord is then briefly discussed, after which the author takes up the various diseases. Here, instead of following the usual method of treatment, he discusses the spinal cord diseases according to their leading symptoms. In the first classification he has those diseases causing symptoms of a transverse lesion of the cord, including in this acute myelitis, abscess, vertebral

disease, tumors, etc.; secondly, he takes those causing atrophic paralysis, both acute and chronic; thirdly, those diseases causing spastic paresis, including in this only primary, lateral, and disseminated sclerosis; and lastly, the diseases in which ataxia is a prominent symptom, including in this the various forms of degeneration in the posterior columns. He has special chapters on spinal meningitis, syphilis, and traumatic affections of the spinal cord. As an appendix he adds the principal methods of pathological examination of the spinal cord, including in this the more important nerve, cell, and neuroglial stains.

In his subject matter the author always assumes a neutral ground; for instance, in the discussion of the causes of tabes he does not commit himself to any particular view, but presents all the different theories, criticising each justly. So it is when discussing the more recent views regarding the centres for the bladder and rectum, in which he assumes that they are probably in the lower portion of the spinal cord, but gives credit to the views of Müller, who believes that they are mostly located in the lower sympathetic ganglia. He fails to make a subdivision of the lower part of the spinal cord into the conus and epiconus, which Minor has recently called attention to, and his chapter on injuries of the cord is too brief. He devotes only two and one-half pages to traumatic neurasthenia and hysteria, a subject which should demand more attention. T. H. W.

#### ERGEBNISSE DER INNEREN MEDIZIN UND KINDERHEILKUNDE.

Herausgegeben VON F. KRAUS, O. MINKOWSKI, FR. MÜLLER, H. SAHLI, A. CZERNY, and O. HEUBNER. Redigiert VON TH. BRUGSCH, of Berlin, L. LANGSTEIN, of Berlin, ERICH MEYER, of Munich, and A. SCHITTENHELM, of Erlangen. Vol. i; pp. 620. Berlin: Julius Springer, 1908.

*Die Ergebnisse der inneren Medizin und Kinderheilkunde* has been evolved from the desire to provide critical discussions of advances in knowledge and present-day opinions of subjects of interest to clinicians in internal medicine in its many aspects. The purpose of the editors, judging from their announcement and the contents of the first volume, is to publish virtual monographs on important topics by those whose inclinations and training make them especially adapted thereto. The projected scope of the publication is sufficiently wide, since it comprises not only the diseases included within its title, but also diagnosis, methods of investigation, such as radiography, bacteriology and serology, general and special therapeutics, general and special biology and pathology, physics, and chemistry. The first volume contains seventeen articles, of which several are

of much interest and importance: The Morgagni-Adams-Stokes symptom complex, by D. Pletnew; digitalis therapy, by Albert Fraenkel; jaundice, by Hans Eppinger; pyloric stenosis in infancy, by J. Ibrahim; the acetone bodies, by A. Magnus-Levy; the treatment of tabes dorsalis, by Frenkel-Heiden; the clinical diagnosis of tuberculosis of the bronchial glands, by O. de la Camp; and pseudo-bulbar paralysis, by George Peritz. Should succeeding volumes maintain the standard set by the first, they unquestionably will be highly prized by clinicians interested in the progress of medicine and critical discussions of the literature. A. K.

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**THE PRINCIPLES AND PRACTICE OF MODERN OTOTOLOGY.** By JOHN M. BARNHILL, M.D., Professor of Otology, Laryngology, and Rhinology in the Indiana University School of Medicine; and ERNEST DEWOLFE WALES, B.S., M.D., Associate Professor of Otology, Laryngology, and Rhinology in the Indiana University School of Medicine. Pp. 575; 305 original illustrations, many in colors. Philadelphia and London: W. B. Saunders Co., 1907.

THE authors of this volume state in their preface that their object has been: (1) To modernize the subject; (2) to correct certain traditional beliefs; (3) to advocate the earliest possible prophylaxis or treatment; (4) to emphasize the importance of a thorough examination and a definite diagnosis as a basis for rational treatment; and (5) to thoroughly illustrate the text. In general, it may be said that they have fulfilled the purposes which they intended. The science of otology is presented in its most modern aspects, and the book is most excellently illustrated. In regard to the second object, "to correct certain traditional beliefs," it may be justly questioned whether anyone who could in any possible way consider himself competent to treat diseases of the ear would require to be told that the old idea "that children would outgrow their aural ailments" is a mistake; and, as to objects three and four, the obvious necessities on which they are based would seem to render it hardly necessary to state them as among the important reasons for writing a new book.

The book is a good practical treatise on diseases of the ear, applicable to the needs of the general practitioner, and also well worth a place in the library of the specialist. The illustrations, particularly the reproductions of anatomical preparations, are especially noteworthy. The descriptions of the operative procedures are excellent, and, while the authors show on every page thorough familiarity with the most modern literature of the subject, they also display much originality, the result of their own large experience.

The book would not be suitable for a text-book for the ordinary

medical student, as the authors' views are so peculiarly their own; but it is eminently adapted for the use of graduates who desire to familiarize themselves with the aspects of modern otology.

F. R. P.

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**PATHOGENIC MICRO-ORGANISMS, INCLUDING BACTERIA AND PROTOZOA.** By WILLIAM H. PARK, M.D., Professor of Bacteriology and Hygiene in the University and Bellevue Hospital Medical College, New York. Assisted by ANNA W. WILLIAMS, M.D., Assistant Director of the Research Laboratory of the Department of Health, New York. Third edition; pp. 648; 176 illustrations. Philadelphia and New York: Lea & Febiger, 1908.

PARK's well-known and excellent *Pathogenic Micro-organisms* has been carefully revised and considerably enlarged so as to permit of the incorporation of the many advances made in our knowledge of bacteria and protozoa during the three years that have elapsed since the publication of the second edition. New sections dealing with the opsonic index, the bacteriology of the normal intestines, and the elimination of the non-antitoxic substances in protective sera, etc., have been added. As in previous editions, special attention is given to the protozoa—the section dealing with these organisms having been thoroughly revised by Dr. Williams. A glossary of some of the newer and more technical terms has also been added. The book excellently fulfils the purpose intended, and may be cordially recommended to student, practitioner, and health officer as a trustworthy guide to the manifold relations of bacteria and protozoa to disease.

A. K.

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**DIE CHRONISCHE PROGRESSIVE SCHWERHÖRIGKEIT, IHRE ERKENNTNIS UND BEHANDLUNG.** By DR. AUGUST LUCÆ. Berlin: Julius Springer, 1907.

THIS monograph is an earnest effort to clear up the obscure and difficult subject of which it treats. Its distinguished author has added to the results of his large clinical experience a most thorough pathological study of the subject, and his work correlates the two. It is needless to say that the conclusions of so eminent an investigator must command the attention of every aurist.

F. R. P.

# PROGRESS OF MEDICAL SCIENCE.

## MEDICINE.

UNDER THE CHARGE OF

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**The Action of Hemostatics in Tuberculous Hemoptysis.**—M. L. GUINARD (*Medical Press and Circular*, 1908, lxxxvi, 316) divides the means employed into three groups: (1) Agents that act on the blood; (2) agents that modify the circulation; and (3) special adjuvants. With the first group comprising many local and general coagulants, the calcium salts, saline solutions, gelatin, and gelatinized serum, the author has had few, if any, good results. In the second group, the vasoconstrictors and vasodilators are taken up at length. The constrictors, such as ergot, ergotin, adrenalin, antipyrin, digitalis, and digitalin, Guinard has tried at different times, but with no promising results. As to vasodilators, amyl nitrite, nitroglycerin, and the nitrites have been used with great success in the treatment of hemoptysis, the first drug especially having been employed by Guinard for the last three years at the Bligny Sanitarium with no untoward symptoms; it acts with great promptness and efficacy. As regards special adjuvants, under which may be classed the counter-irritants, physical agents, and sedatives, ice has at times been most useful, and in Guinard's experience morphine occupies the foremost place.

In connection with this article on hemoptysis there is another on the uses of amyl nitrite by GEORGE A. GRACE-CALVERT (*Brit. Jour. Tuberculosis*, 1908, ii, 189), who reviews the many previous reports for and against the use of this drug in hemoptysis, in most of which the authors agree that it is of great value in some cases; it may be followed or accompanied by the other general measures for the relief of the trouble. Calvert concludes that the following points are in favor of amyl-nitrite. It acts instantly, producing an immediate fall in blood pressure at the bleeding points, thus giving time for clotting to take place, while the bleeding usually ceases at once. It apparently produces an intense

anemia of the lung parenchyma without any reactionary hyperemia, such as follows the use of adrenalin. The capsules can easily be carried by the patient, who can then inhale the contents of one as soon as the hemoptysis begins, thus starting in the treatment at once and often preventing a worse attack. Calvert considers this drug, then, to be the most efficient of all in the treatment of such cases and by far the best one to administer first.

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**Sodium Chloride and the Gastric Secretion.**—A. MARTINET (*Presse médicale*, 1908, liii, 418) notes that there are two actions of salt: one local on the mucous membranes of the mouth and stomach; and a general action exercised after its absorption into the body. As regards the local action, many authors say that the HCl and the peptic digestion are both diminished by the action of salt, while, on the other hand, some authors assert that these functions are increased. These differences are better understood when it is known that most of the previous work has been done on animals either carnivorous or herbivorous by nature, whereas, in man, who is omnivorous, the conditions are very different. The inhibiting or stimulating local action depends much on the habits, the anomalies of the gastric secretion, the food, and according as the salt is given alone or mixed with food. As regards the general action following prolonged feeding on a salt or salt-free diet, the views are more unanimous that the long-continued use of salt leads to a hyperchlorhydria; that a salt-free diet leads to a hypochlorhydria and diminishes the gastric secretion. Clinically, it is well known that the prolonged suppression of salt in the diet produces pain and vomiting in conditions of hyperacidity, while in other conditions in which the HCl is deficient the use of salt increases it and aids digestion greatly. Martinet's experiments on a healthy man, following out L. Meunier's technique, showed that with certain foods, as meat, the digestion was the same with or without salt, but with other foods, such as milk, eggs, and carbohydrate food stuffs, the digestion was delayed from ten to twenty minutes when no salt was given with them. He therefore concludes that in certain subjects and with certain foodstuffs, the addition of sodium chloride to the diet favors the gastric secretion.

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**Hydremia in Nephritis.**—HALPERN (*Deut. Arch. f. klin. Med.*, 1908, xciii, 585) has made an extensive study of the hydremia of nephritis. He finds in cases of chronic parenchymatous nephritis, in which the kidneys are compensating fully, that the quantity of water, nitrogen, and chlorides remains normal in both plasma and red blood cells. Even with oedema the solids of the blood may be normal, but the plasma is diluted and is relatively increased as compared with the red blood cells. Hydremia without dilution of the plasma affects cases without oedema, and depends on the increased amount of plasma as compared with the red blood cells. Hydremia with dilution of the plasma is found particularly in oedematous patients and is due principally to the retention of water. In the course of chronic parenchymatous nephritis Halpern usually finds the sodium chloride practically normal in the plasma and in the red blood cells—the relative amounts of this salt in the corpuscles and plasma being as 1 to 2 in health, but this ratio may be altered to 1 to 5.

**An Experimental Investigation into the Functions of the Thymus Gland.—**

ALEX. MACLENNAN (*Glasgow Med. Jour.*, 1908, lxx, 97) reviews some of the previous work done on this subject and gives the results of his operative measures on animals. He concludes that the thymus, though it may be a lymphatic gland, yet is so specialized that it must have an internal secretion of more or less importance to some of the various functions of the body. The gland is an accessory one, for its functions may be taken up by others without apparent disturbance to the individual; however, the simultaneous removal of the thymus and spleen always results in sudden death, thus suggesting that the spleen itself may carry on at times the functions of the thymus. The thyroid and the thymus are closely associated in many ways, and the results in experiments have shown that the thymus is unnecessary to the general economy when the thyroid is gone, and when the thymus is removed less thyroid suffices. The importance of this relationship is apparent in certain diseases. The sudden death in some cases of Basedow's disease following thyroidectomy, in which the thymus has subsequently been found to have been enlarged, is important on account of the relation of the enlarged thymus and the condition of status lymphaticus; the enlarged thymus after removal of the thyroid gives rise to the same conditions as produce the so-called thymus death. Therefore, in cases in which thyroidectomy is necessary an enlarged thymus should first be sought out and removed before the thyroid is extirpated.

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**Polycythemia, Erythrocytosis, and Erythema.**—F. PARKES WEBER (*Quarterly Med. Jour.*, 1908, ii, 85) in an exhaustive critical review first divides the cases of absolute polycythemia into two divisions: (a) apparently primary cases of hyperplasia of the red cells, that is, cases of erythema; and (b) secondary or symptomatic cases of hyperplasia of the red cells, that is, cases of erythrocytosis. The first condition (a) is exemplified in those cases in which the persistent relation and absolute polycythemia is due to an excessive erythroblastic activity of the bone marrow, which appears to be the primary morbid picture in a condition which is characterized by a persistent increase in the viscosity and total volume of the blood, cyanosis, and enlargement of the spleen. The second condition (b) is one in which the erythrocytosis is an effort on the part of the organism to compensate for some difficulty in the oxygenation of the blood and tissues of the body. Thus, erythrocytosis may be looked upon as analogous to a leukocytosis, and in all cases of erythrocytosis there is as much cause for the hyperplasia of the red blood corpuscles as in cases of renal and cardiac disease there is for the heart to become hypertrophied. As conditions inducing the second group may be mentioned residence at high altitudes and chronic cardiac and pulmonary complaints. Weber then goes into the various causes of the polycythemia in cases of erythrocytosis and in those of erythema, and the character of the blood and blood-forming tissue in absolute polycythemia. The condition of erythema is next considered in detail. As regards its pathology and etiology, the various hypotheses as to its being due to a primary disease of the bone marrow, increased durability of the red blood cells, diminished oxygen capacity of the hemoglobin, or possibly to toxic and infectious causes, are discussed, the prevailing theory being that the polycythemia

is due to a "primary" myelopathy; the question of impeded circulation (blood stasis) as a primary cause for the polycythemia has, however, been seriously considered. As regards treatment the various measures advocated are detailed. Venesection, splenectomy, x-rays, and many drugs have been used, most of which have had little or no satisfactory effect. The plentiful use of German "sour milk" or some similar preparation, on account of the effect on the flora of the large intestine, might be worth a trial in some cases, and a lacto-vegetarian diet, or one rendered as poor in iron as possible, has likewise been suggested.

**Pernicious Anemia and Renal Lesions.**—M. LABBE and E. JOLTRAIN (*Arch. des maladies du cœur, des vaisseaux, et du sang*, 1908, i, 366) note that relations between pernicious anemia and renal lesions have been suggested lately, and report the following case: A man, aged fifty-two years, came under treatment for a grave anemia, weakness, and generalized edema. The patient grew steadily worse, and died in apparently uremic coma. The examination of the blood showed an intense plastic anemia with myeloid reaction and hyperleukocytosis; some nucleated reds were present and the corpuscular resistance was normal. At autopsy the main lesion present was nephritis with a kidney of the large white type. The factors of dilution of the blood, toxic hemolysis, or a defect in the corpuscular resistance, the author does not think can enter into this case. It is possible, however, that both the renal and blood lesions are the result of some infection or intoxication. At any rate, this association of the two lesions is frequent and should be noted in a condition the cause of which is so often unknown. The diagnosis between Bright's disease and pernicious anemia at times is very difficult, and a careful examination of the blood in all nephritics may help to distinguish the yellowish color of the skin of one condition from that of the other; one should bear in mind the possibility that both conditions may exist as a pathological syndrome in the same individual.

**Arterial Hypertension with Hyperplasia of the Pituitary and Suprarenals.**—J. PARISOT (*Arch. des maladies du cœur, des vaisseaux, et du sang*, 1908, i, 426) discusses those cases in which there is increased blood pressure and consequent cardiac hypertrophy in the absence of lesions in the kidneys, the condition depending apparently on the hyperplasia of two blood pressure raising organs, the pituitary and the suprarenals. He reports a case in a young girl, aged twenty-two years, who had been perfectly healthy up to a period six months before her death. Then symptoms of amenorrhœa and ovarian trouble began, followed gradually to the time of admission to the hospital by evidences of increasing cardiac hypertrophy, arteriosclerosis, and great hypertension. There were also cerebral disturbances due to increased intracranial pressure. At autopsy the kidneys were perfectly normal, the heart much hypertrophied, while the pituitary and suprarenals showed great hyperplasia. The ovaries showed some cystic degeneration. The known relation of degeneration and atrophic conditions of the ovaries and testicles to hyperplasia of the suprarenals, as pointed out by other authors, leads Parisot to suggest that the ovarian lesion was probably the primary cause of the increased functioning of the suprarenals and



pituitary which led gradually to the cardiac and arterial changes from which the patient died.

**Gastromyrorrhoea.**—JULIUS FRIEDENWALD (*Boston Med. and Surg. Jour.*, 1908, lix, 265) observes that the presence of small quantities of mucus in the fasting stomach has been frequently noted. This normally should not exceed 5 cm., and when above 25 cm. Kuttner considers it indicative of the condition of gastromyrorrhoea. The diagnosis is, however, justified only when the mucus is constantly present or appears at certain intervals in patients who are unaccustomed to the use and manipulations of the stomach tube. Otherwise the action of the tube itself may account for secretion of mucus. There are two forms of this disease, the intermittent and the continuous. In the first the patient is comparatively well during the intervals between the attacks, which come on, as a rule, suddenly, with severe headache, pain, and vomiting, the latter condition being quite intractable; no food or medicine can be retained, and after a period varying from one to five days, and in one case even up to twelve days, the attack suddenly ceases. In the other type there are no characteristic symptoms and it is usually discovered in examination for other conditions of the stomach, as chronic catarrh, conditions with an absence or diminution of HCl, etc. As regards treatment, lavage seems to be of some service at the beginning of an acute attack, but not later. In the chronic form it is of some help, as is also the free administration of mineral waters. Other symptomatic measures may be used during an attack, and in the interval measures should be employed to correct as far as possible the neurotic tendency, which is marked in some cases. In association with the above abstracted article on the hypersecretion of mucus, the same affection of the intestinal tract is the subject of an article by L. Cheinisse (*Semaine médicale*, 1908, xxviii, 385), on enteromyrorrhoea of nervous origin, in which he reviews the literature of the subject and reports some cases in detail. As regards the etiology of this, as in the previous condition, the nervous element seems to play an important part, some patients having also had obstinate constipation of long standing. It is of importance to distinguish this form of the disease with its absence or scantiness of formed elements and excessive amount of thin mucus, the patient experiencing no pain, from those cases of mucous colitis in which the evacuation of mucus often formed and in casts, preceded generally by pain, are the striking symptoms. In the treatment of this disease the nervous condition of the patient must be carefully considered. The bowels must at first be thoroughly cleansed, and after a rest of a few days flushed with mild astringent enemas.

**Comparative Experiments on the Presence of Complement-binding Substances in the Serum and Urine of Syphilitics.**—UDO J. WILE (*Jour. Amer. Med. Assoc.*, 1908, li, 1142). The great amount of work recently done on the blood of syphilitics with the Wassermann reaction successfully has led to a finding of the same complement-binding substances in the milk of syphilitic women, and in a preliminary report Wile and a co-worker have demonstrated the same reaction in the urine of syphilitic patients. In this paper the results of the investigations of 100 cases

in which the serum and urine were tested is given, so that the relative value of each in the diagnosis of syphilis could be compared. Wile concludes as follows: The urine in a large percentage of cases of syphilis contains substances which behave in the same way as the antibodies in the serum of the same cases. These substances seem to appear a little later in the urine than in the serum, and at times are present in one and not in the other, and vice versa. The diagnostic value of the reaction in the urine must for the present be viewed with caution, inasmuch as 2 per cent. of our total number of cases gave a positive reaction in the urine, while the serum in these cases was negative. In both serum and urine these bodies tend to disappear under vigorous antisyphilitic treatment.

**The Serum Diagnosis of Syphilis in Mental Affections.**—G. RAVIAT, M. BRETON, G. PETIT, M. GAYET, CANNAC (*Presse médicale*, 1908, lxxi, 564). The importance of syphilis as an etiological fact in so many cerebral and cord lesions has led the authors to perform the Wassermann test in 400 persons suffering with such disturbances. Of these, 165 gave positive reactions and 235 negative. Of 72 patients with general paralysis, 13 giving a history of lues, there were 93 positive and 7 negative reactions. All the cases in general paralysis and tabes reacted positively. Of the acutely demented cases the reaction was not so common. Thus, in dementia præcox, 26 per cent. were positive; in organic dementia, 30 per cent. positive. In cases of arrested mental development, such as idiots and imbeciles, the positive reactions occurred in from 30 to 34 per cent. In 234 cases with some stigmata of hereditary lues, only about 16 per cent. gave negative reactions, and in many of these there was the possibility of the glandular or ocular manifestations not being luetic. In conclusion, the authors, as a result of these positive and negative tests, wish to note the importance of lues as an etiological factor in general paralysis and tabes, and, to a lesser degree, dementia præcox, organic senile dementia, and finally in epileptics, in which latter there were the fewest positive reactions. In the imbeciles and idiots the importance of lues in their etiology is shown by the frequent positive reactions, which occurred in about one-third of the cases.

## SURGERY.

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**Cancer of the Mouth and Tongue.**—WARREN (*Annals of Surgery*, 1908, xlviii, 481) says that the relation of the lymphatic system to the primary growth is the most important anatomical consideration in operations for

cancer of the mouth and tongue. Persistent chronic inflammatory processes of the mucous membrane predispose to cancer, and should be treated surgically. Cancer of the mouth and tongue is limited locally and to the adjacent lymphatic system. Internal metastases are rare. Microscopic diagnosis is the crucial test in doubtful cases, and should be made at the time of operation. Antisymphilitic treatment is not a sure guide, and should not cause delay in operation. Modern operative treatment involves: preliminary treatment of the mouth; protection of the respiratory tract by drugs, intubation of the pharynx, or laryngotomy, or by position; removal of the primary lesion with a margin of one inch, if possible, of healthy tissue; block dissection of the lymphatic bearing tissues of the anterior cervical triangle, on one or both sides, as a routine measure. A lower mortality may be obtained by the block dissection of the neck as a secondary operation, about two weeks after the excision of the primary disease. The intrabuccal operation is inadequate to reach the entire operative field, and should be supplemented by a dissection of one or both anterior cervical triangles. The ideal operation of the future should contemplate a free exposure of the mouth and anterior cervical triangles as one continuous area with a block dissection of its diseased contents. The mortality varies with the extent of the operation, and is lowest (5 per cent.) with the intrabuccal operation, and highest (30 to 35 per cent.) in the operations involving division or resection of the lower jaw. Death is, as a rule, attributable to shock, sepsis, or bronchopneumonia. In a series of cases taken consecutively from the records of the Massachusetts General Hospital, 112 operations upon cancer of the tongue and mouth resulted in 16 cases free from recurrence over three years after operation (14.2 per cent.) (all supported by pathological examination of the tissue). Of 57 cases of the tongue, 10, or 17.5 per cent., were cured by operation. Local recurrence of the disease occurred more often than recurrence in the lymphatic glands alone. In only one case did recurrence make its appearance at a period of more than three years after operation.

#### **The Operative Treatment of Gunshot Wounds of the Spinal Cord.—**

BRAUN (*Deut. Ztschr. f. Chir.*, 1908, xclv, 115) says that operation is indicated when there is reason to suppose that the bullet (splinters, cicatricial tissue, callus, etc.) in the spinal canal is projecting into the cord or producing an irritating process about the cord; and the functional disturbances, in part at least, can be accounted for by compression or irritation. Except in those cases in which a comminuted fracture or a hemorrhage with threatening infection compels an early operation, the indication, according to our present views, is to delay operation until we can determine the extent to which there will be a spontaneous return of function and until a topical and anatomical diagnosis can be made. The gravity of the cord lesion is the decisive factor. Mild cases with early moderate or rapidly improving symptoms should not be operated on. Missiles have often been fruitlessly searched for and have been falsely localized. The smaller the missile the longer one should wait for a subsidence of the symptoms. Small bullets can often find sufficient room near the cord, and the diagnosis of their presence, when not associated with severe lesions of the cord, may be very difficult or even impossible. Small shot may heal in permanently, in the substance of the cord,

without reaction. The larger the missile or the splinter the greater the probability of finding it quickly and the greater the danger of secondary disturbances from it, as infection or irritation. The operation is indicated in cases with severe cord lesions showing slow improvement or cessation of it, due to intradural or extradural foreign bodies pressing upon or irritating the cord. The fear of the existence of a total transverse lesion does not contra-indicate operation, and one should not wait too long before operating in such cases. The operation should be done under most favorable conditions, upon the basis of a good skiagraph and a careful diagnosis of the segment of the cord involved. Only then could the unquestionable inherent dangers of the operation be successfully avoided. Braun thinks that the osteoplastic methods of doing laminectomy are not advisable, particularly in gunshot wounds of the cord. The raising of such a flap, which includes the laminæ, would considerably endanger the cord because of the adherent and probably lacerated dura. Moreover, the danger would be greater from the more or less fractured and splintered canal, which condition was present in many of the cases. After exposing the vertebrae he would first remove the spinous processes, open up the canal by removing an uninvolved lamina, and then would bite away step by step the involved laminæ, first with small and then with large gouge forceps. This operation is time consuming, but without danger, and does not shake up the cord, as would the blows upon a chisel. Under aseptic conditions he would close the wound, with the introduction of one or two drains, which could be removed in four days. If infection were present, he would employ the open wound treatment, with drainage and gauze packing.

**A New Method of Producing Local Anesthesia in the Extremities.**—BIER (*Archiv f. klin. Chir.*, 1908, lxxvi, 1007) introduced novocain into the circulation for the production of local anesthesia in an old case of tuberculosis of the elbow. By means of an Esmarch bandage applied from the fingers to above the elbow, the blood was pressed out of the limb. Then tourniquets were applied four fingers' breadth above and the same distance below the elbow. The median vein at the elbow was then exposed under Schleich's infiltration method of anesthesia. As in intravenous infusion, a cannula was introduced peripheralward through a slit in the vein and held by a ligature. The vein was then ligated on the cardiac side, and with the usual infusion instrument 10 c.c. of a 0.25 per cent. novocain solution were injected into the vein. The valves in the veins offered only slight resistance to the passage of the fluid throughout the portion of the limb included between the tourniquets. Immediately after the injection was ended the previously very stiff and painful joint could be moved without pain. The resection was then begun. The incision through the skin, muscles, and periosteum was without pain. The lifting of the periosteum was at first complained of, but soon it was not noticed. The extirpation of the capsule, sawing of the bone ends, and excision of the fistulous tracts were likewise painless. That the condition was a very painful one was seen from the loud outcries on the preliminary injections of the Schleich fluid. At the termination of the resection, one-quarter hour after the injection of the novocain solution, the sensation below the peripheral tourniquet was tested. It was absent throughout the whole part, but motion was not. Twenty

minutes after the introduction of the novocain the operation was ended. The peripheral tourniquet was then removed and the central one loosened to such a degree that the arteries were opened but the veins still kept closed. The novocain was thus prevented from entering the general circulation. Then the tourniquet was again tightened, and after completion of the packing of the wound it was completely removed. After seven minutes sensation returned on the flexor surface, and after two minutes more on the extensor surface. The same method was employed with equal success in a necrotomy of the lower two-thirds of the radius.

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**The Operative Treatment of Lung Abscess.**—PERTHES (*Archiv f. klin. Chir.*, 1908, lxxxvi, 1054) says that the results obtained from operation for chronic lung abscess are not as good as those from the acute form. Acute and chronic abscess of the lung have much the same relation to each other as recent and old empyemas. While simple pneumotomy in acute abscess of the lung usually heals without fistula, this is not the case with the chronic form. Our treatment in acute cases is well established upon the basis of large numbers of cases, but this is scarcely so of the chronic. The latter is usually a continuation of an acute case. Drainage by expectoration through an opened bronchus is not sufficiently free, and re-accumulation repeatedly occurs, or the abscess is too large to permit collapse of its walls after the evacuation of its contents. The walls become callous, and not rarely new abscesses develop in the neighborhood of the original. It is best in these cases to open and drain the abscess first by a pneumotomy. The removal of the abscess wall should be deferred to a later period, when the general condition of the patient will be improved. The original pneumotomy for the opening of the abscess cavity should be done in two stages. In the first, the ribs should be resected and the visceral and parietal pleuræ attached to each other by sutures under anesthesia. The second stage, carried out a few days later, consists in locating the abscess from the wound by puncture and in opening it without narcosis. The later operation consists in removing the abscess. This is done by extirpation of the whole abscess wall, with the application of the skin and muscle chest flap upon the lung wound.

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**A New Treatment for Old Tubercular Sinuses.**—RIDLON and BLANCHARD (*Amer. Jour. Orthop. Surg.*, 1908, vi, 13) report the results in 26 cases, in which Beck's bismuth-vaseline paste was employed for the treatment of old tubercular sinuses. Beck used two mixtures. The first consisted of bismuth subnitrate 1 part, and vaseline 2 parts. These were mixed while boiling, and the mixture was injected into the sinuses for the purpose of obtaining a clearly outlined skiagram of the track of the sinuses. The second mixture differed only slightly from the first, and consisted of bismuth subnitrate, 6 parts; white wax, 1 part; soft paraffin, 1 part; and vaseline, 12 parts. In most of the 26 cases the first mixture was injected and evacuated within twenty-four hours. The second was then injected into the fistula until it would hold no more without painful distention. The temperature of the paste was high enough to give it the consistency of cream. The cases were divided into three groups. In the first, the opening of the fistula healed over in from one to three weeks, and the fistula was cured with the bismuth paste partially retained. In the

second group the results were only partly favorable, owing to the extensive bone destruction, leaving many ramifying sinuses. Injections were made three times a week. In two or three weeks the pus was changed to a transparent viscid fluid, giving assurance that after months of persistent treatment the sinuses may be cured. In the third group, the negative cases, there was extensive bone destruction, with retained sequestræ and ramifying pockets, so deeply and peculiarly situated that the bismuth paste could not be forced into them, and, therefore, the pus could not be displaced from them. The theory offered by the writers for the action of bismuth-vaseline paste, is that: (1) The material acts as a plug forcing and squeezing out the pus; (2) it so completely fills the sinus as to prevent the ingress of germ laden air; and (3) it compresses the unhealthy granulating surfaces and favors a normal healing process. Of the 17 cases of tubercular sinuses at first treated with this injection material, 9 were cured in from seven to thirty-three days, while 7 of the remaining 8 were more or less improved at the end of three months. Four large tubercular abscesses, two psoas and two hip, were opened, evacuated, and filled with the bismuth paste. This was followed by a discharge of transparent serum, which diminished, after three or four days, to 10 or 15 drops a day. This serous discharge remained absolutely sterile and after a few days ceased altogether. There was no rise of temperature or other untoward symptom in either case, and the writers believe that the problem of opening tubercular abscesses and keeping the cavities sterile, has been solved. Six of the cases had been under the tuberculin treatment by the Wright method for one and one-fourth years, with no notable change in either the quality or quantity of the pus discharged from the several sinuses. Two of the 6 sinus cases have since been cured and the other 4 so much improved under the bismuth-paste treatment as to give promise of ultimate cure. The closing of the sinuses does not imply any relaxation of the mechanical and other treatments in cases of progressing tubercular joint disease.

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**The Influence of Weight-bearing on the Treatment of Tubercular Hip-joint Disease.**—GIBNEY (*Amer. Jour. Orthop. Surg.*, 1908, 21) says that from 1884 to the present time he has had a large experience with the ambulatory traction hip splint in all of its modifications except those which allow motion at the joint. Yet immobilization has always appealed to him. The late Hugh Owen Thomas claimed the best results from immobilization, with and without the use of the limb, that is, crutches and a high shoe in the more active stages of the disease, and without these aids in the less active stages. Pathologically considered, it would seem that the weight of the body should never be considered as safe until one is assured that all active disease, all exacerbations, have passed. Gibney's clinical experience in the last few years, however, has led him to believe that the danger is a fancied one and not real. He thinks that if the motion of the affected joint is put out of action, the weight of the body in walking may be useful rather than harmful, and he offers the reports of a few cases in corroboration of this view. The first case was one of hip disease of rather acute invasion. There were rather extensive changes in the head and neck, as shown by the x-rays, and deformity. Traction was employed at first, but fixation by a short plaster-of-Paris spica bandage, with use of the limb, was employed

during the greater period of treatment. After about four and one-half years of this treatment the result was almost perfect. Seven other cases were treated in a similar manner, with excellent results, although not a complete cure in all.

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**Death following Spinal Anesthesia with Stovaine.**—HARDOUIN (*Arch. gén. d. chir.*, 1908, ii, 115) reports a death in his practice from this method of anesthesia, and the results of a study of 16 fatal cases collected from the literature. There is much difference in opinion among writers who employ stovaine by lumbar injection. Hardouin considers that it is contra-indicated in the aged and the feeble and in children. Even its warm partisans admit the necessity of having ready the material for intravenous infusion of artificial serum, also caffeine and ether, so that the method is absolutely impracticable in emergency surgery outside of a hospital. It should be reserved for those cases in which chloroform is contra-indicated and in those in which local anesthesia is insufficient. While Hardouin recognizes its value in some cases, his study of the subject does not permit him to say that it is without danger. He believes that his case belongs in the list of those for which the method is contra-indicated. Yet he prefers to give up its use rather than expose himself to the danger of overlooking a contra-indication which may be difficult to recognize. He strongly objects to using spinal anesthesia with stovaine unless chloroform or local anesthesia is contra-indicated.

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**Two Cases of Stricture of the Prostatic Urethra.**—ANDRE (*Ann. d. mal. d. org. génito-urin.*, 1908, ii, 1041) says that while these strictures have been reported, they are still rare, and further reports are desirable. He records two cases, the only ones he has ever seen, in a large experience in genito-urinary diseases, and these he saw a few days apart. Both occurred in old men, one aged sixty-six years, the other aged seventy-two years, so that some doubt arises as to whether they were not obstructions due to prostatic enlargements. In the first case he was called on account of acute retention. There had been difficulty in urination for several years, and the patient some time previously had been passing on himself from time to time a No. 14 conical bougie, but had not continued to do so. A No. 23 sound passed easily through the anterior urethra, but stopped at the prostate. Digital examination through the rectum showed the prostate to be as large as a mandarin. Thinking that the urethra had deviated because of the hypertrophy of the prostate, various catheters were tried, some soft with a staff, and others metallic with large curve, but all without effect. They became engaged about 2 cm. in the prostate and could progress no farther. Small sounds and filiform bougies were also tried without success. To relieve the retention suprapubic tapping was done morning and evening, for three days. Finally, on the third day, a filiform was passed and tied in position. The next day a No. 10 sound was passed. The size was increased every few days until No. 20 was reached. With all these sounds there could be felt, in passing the prostate, a gripping of the instrument in a hard, fibrous ring, difficult to dilate. Finally, after some months a No. 23 was passed. The patient now urinates very well, and empties the bladder almost completely in spite of the enlarged prostate, and his general condition has improved very much. The patient never sustained any injury in this

region. In the second case the difficulty in urination had been supposed for some years to be due to the enlarged prostate, but the increasing difficulty and pain from passing a No. 13 or 14 catheter suggested a tightening stricture of the posterior urethra. The prostate was much enlarged. Internal urethrotomy was done and a permanent catheter left in for six days. A No. 20 sound was passed afterward, as often as was necessary. After a cure of six months duration the caliber of the urethra again began to decrease and was kept open only with considerable difficulty.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**Local Use of Magnesium Sulphate Solution in Erysipelas.**—TUCKER (*Therapeutic Gazette*, 1908, vi, 381) reports excellent results in 19 cases of erysipelas complicating both medical and surgical cases. In 35 uncomplicated, though severe, cases, all recovered within two to seven days, and the pain and usual local discomfort was relieved in a few hours. In the entire series no internal treatment was employed, unless indicated by some complication. He employs a saturated aqueous solution of magnesium sulphate. This is applied on a mask consisting of 15 to 20 thicknesses of ordinary gauze, extending well beyond the area involved. A small opening is left for the nostrils, but none for the eyes. The mask is covered with oiled silk or wax paper and kept constantly wet. The dressing is not to be removed oftener than once every twelve hours, and then only for inspection of the parts. Tucker claims the advantages of this form of treatment over others are as follows: It is easily obtained and easily made into solution; it is non-toxic, inexpensive, clean, and easy to apply; it promptly allays the pain and discomfort; the temperature rapidly falls to normal usually during the second twenty-four hours and remains down; it lessens the liability to serious complications; there is no necessity for internal medication. Tucker has also used this treatment in over 700 cases of various forms of inflammation, and considers it the best form of local treatment for such conditions.

**The Practical Application of the Salt-poor Diet.**—STRAUSS (*Ztschr. f. Phys. und diät. Therap.*, 1908, xix, 14) discusses the best methods of reducing the amount of salt in a mixed diet. This matter is of considerable practical importance, since a salt-poor diet is now recommended in certain cases of nephritis and of heart disease. A similar diet has been used in diabetes insipidus with good results. In epilepsy a salt-poor diet has been an aid in carrying out a long course of bromide treatment. For the proper prescribing of such a diet it is necessary to possess a knowledge of the amount of salt contained in the ordinary articles of



food, both in their natural state and as ordinarily prepared for the table. Strauss presents such comparative lists, and the following examples may point out the practical advantage of such a knowledge: Milk contains 0.15 to 0.18 per cent. of salt; salted butter, 1 per cent.; unsalted butter, 0.02 per cent.; cheese, usually from 1.5 to 2.5 per cent.; eggs, 0.14 per cent.; white of egg, 0.19 per cent.; egg yolk, 0.02 per cent.; and meat, 0.1 per cent. Corn and legumes (except lentils, which contain 0.23 per cent.) contain 0.01 to 0.1 per cent. Most of the other vegetables contain about 0.1 per cent. Spinach (0.21 per cent.) and celery (0.31 per cent.) contain more than the average. Fruit usually contains less than 0.06 per cent. The following partial list shows the importance of methods of cooking. Thus, poached eggs contain 0.5 per cent. of salt, while scrambled eggs and omelets contain from 2.4 to 2.7 per cent. Roast beef contains from 1.9 to 2.8 per cent., and beef stew 3 per cent. White bread contains from 0.48 to 0.7 per cent., and brown bread 0.75 per cent. Cooked cauliflower and mashed potatoes contain about 0.5 per cent., while asparagus contains 2.7 to 3.5 per cent. In general, Strauss states that those articles are to be avoided which need to be cooked with salt in order to be palatable. This means a limitation in meats and meat broths. Since these are usually forbidden in the conditions for which this diet is available, this is not an added hardship. This deficiency in proteid caused by excluding meat preparations is met by the use of proteid foods which need little or no salt in their preparation. Such foods are milk, cheese, and eggs in various forms. Poached eggs and scrambled eggs can be made palatable without salt. Various sauces, made with flour and sweet butter, add to their palatability. The carbohydrates are supplied by bread made without salt, puddings, various forms of pastry, fruit cooked with sugar, etc. Bread is of great importance in a salt-poor diet, because when the amount of meat is limited larger quantities of bread will be taken. Though the unsalted bread has a sweetish taste, it is not unpleasant with unsalted butter or marmalade. Various vegetables may be given, because they introduce variety into the diet and because they form vehicles for flour and especially fat. Strauss does not recommend the salt-poor diet for all cases of nephritis, but only when there is dropsy or a tendency to dropsy. He makes use of a "trial diet" which consists of one-half liter of coffee and milk, one liter of milk, one-fourth liter of a milk soup, 2 eggs, 80 grams of butter, 80 grams of beef, 4 rolls. A normal person should excrete 7 to 9 grams of salt on this diet. This trial diet should be given to the suspected case of nephritis. If there results a considerable discrepancy from the theoretical excretion of salt, it would indicate a tendency to dropsy if it did not already exist. In cases of heart disease a moderate limitation in the amount of salt is generally sufficient. A rigid treatment is necessary only when there is marked degeneration of the kidney resulting from long-standing congestion.

**Exclusive Milk Diet in the Treatment of Obesity.**—MORITZ (*Münch med. Woch.*, 1908, xxx, 1569) has found an exclusive milk diet extremely effectual in the treatment of obesity. He cites 8 cases, mostly in private practice, which prevented a more careful study of the metabolism. The patients lost from 2.4 to 21 kilograms in from 6 to 81 days. He allows from three to five pints of milk daily in five portions. For breakfast

a pint is given, at 10 A.M. a glass, at noon a pint, at 4 P.M. a glass, and at 7 P.M. another pint. The milk may be given warm or cold, and as much as a pint of water may be added to the daily quota. In order to vary the diet, one of the fermented forms of milk may be given. This method obviates thirst and hunger and possesses another advantage in its low percentage of salt content. Thus, it adds a favorable influence on heart and kidney complications. In Moritz's cases the heart disturbances subsided, the pulse rate became lower, and the pulse tension fell. Some of the cases had constipation, which he treated by simple laxatives. When the weight dropped too rapidly, headache and general depression seemed to occur. The patients should preferably remain quiet while on the diet; this lessens the liability to unfavorable symptoms. He estimates the amount of overweight by the difference between the actual weight and a theoretical normal weight. He says a normal person should weigh as many kilograms as his height in centimeters exceeds 100. Thus, a man 168 cm. in height should normally weigh 68 kilograms. He reckons the caloric value of the food with relation to this theoretical normal weight. In his cases he used 16 to 17 calories per kilogram. Since there are about 16.2 calories in 25 c.c. of milk, one can easily obtain the total quantity of milk required in the individual case by multiplying the weight in kilos by 25.

In the first few days most of the loss in weight is due to loss of water. Careful nitrogen determinations were made in one case, over a period of forty-eight days, in order to estimate a possible loss of body proteid. Moritz found that 88.9 grams of nitrogen were lost during the time. These 88.9 grams of nitrogen represent 555.6 grams of albumin or 2920 grams of muscle. The total loss of weight during this same period was 12,500 grams, the difference presumably being water and fat. Both the loss of proteid and fat furnish additional calories to the body. In this particular case these calories from the body proteids and fats added to the calories contained in the milk taken amounted to 38 to 40 calories per kilo of the normal weight. Von Dapper and von Noorden maintain that the proteid loss can be avoided if the proteid percentage of the diet is raised. Von Dapper says that this loss can be avoided when the proteid of the food forms 30 to 40 per cent. of its total caloric value. The proteid of milk forms only about 20 per cent. of its caloric value. Moritz experimented with the addition of nutrose to the milk and raised the proteid in the food to about 26 per cent. of the total caloric value. This was done in only one case, but in this case the proteid loss increased instead of diminished, as would be theoretically expected. Moritz believes that much useful information can be obtained by further observations with this milk diet. He commends above all its simplicity both for the patient and the physician.

**Serum Treatment of Epidemic Cerebrospinal Meningitis.**—FLEXNER and JOBLING (*Jour. Exper. Med.*, 1908, i, 141) state that the administration of their antiserum by direct injection into the spinal canal was based upon some observations first made by Flexner. He noticed that normal sera and sterile exudates had a bactericidal effect upon *Diplococcus intracellularis*. Furthermore, he was able to determine a curative action when a prepared antiserum was brought into immediate contact with the focus of infection in guinea-pigs and monkeys infected with the

diplococcus. Flexner and Jobling state that the serum should be injected directly into the spinal canal in order to secure a restraint of growth at the site of infection. They consider this bactericidal action of more importance than some theoretical objections based on the fact that the destruction of the meningococci liberates their endotoxin. There is experimental evidence to show that the antiserum possesses a certain antitoxic value, since it can neutralize the toxic substance of autolysates of the diplococcus. They believe that the serum increases the phagocytic power of the leukocytes or renders the diplococcus more subject to phagocytic digestion. They also think it probable that the phagocytes not only prevent further multiplication of the diplococci, but also detoxicate the endotoxin by reducing it to non-toxic or less toxic compounds. The fact that colloids and even crystalloids are eliminated from the blood into the cerebrospinal fluid very slowly and imperfectly is an additional reason for the intraspinal injection. The serum is obtained from horses which have been inoculated subcutaneously. The process of immunization may take a year or more. Alternate inoculation of living meningococci and autolysates are made at seven-day intervals. They give the following instructions for the use of the serum: (1) The serum should be kept in a refrigerator until it is to be used, when it should be warmed to the body temperature before it is injected. (2) The serum should be injected directly into the spinal canal after the withdrawal of cerebrospinal fluid by lumbar puncture. (3) The quantity of serum for a single injection should not exceed 30 c.c. It is desirable, although not apparently essential, to withdraw from the spinal canal at least as much fluid as the amount of serum to be injected. The injection should be made very slowly, especially when the quantity of cerebrospinal fluid withdrawn is less than the amount of the serum to be injected. (4) The injection should be repeated every twenty-four hours for three or four days or longer. (5) In general, the earlier in the disease the injections are made, the better the results. Therefore, injections should be made when film preparations show intracellular Gram-negative diplococci. If the culture should show later that the disease is not epidemic meningitis, no harm will result from the injection. (6) Although the best results have been obtained when the injections have been made early in the disease, no case should be considered hopeless. It seems useless to employ the serum in the very late cases when chronic hydrocephalus has developed.

The authors give the detailed histories of the cases treated with the serum and discuss the probable effect of the serum in the individual cases. These cases are included in the following analysis.

**An Analysis of Four Hundred Cases of Epidemic Meningitis Treated with Antimeningitis Serum.**—FLEXNER and JOBLING (*Jour. Exper. Med.*, 1908, v, 690) give the results which were obtained in over 400 cases of epidemic meningitis treated with the antimeningitis serum. These cases occurred in different and widely separated parts of the United States, Canada, and Great Britain. Some of the cases were in small epidemics, while others occurred sporadically. In all of the cases a definite bacteriological diagnosis was made. Under all other forms of treatment the mortality of the disease in the past has been in the height of epidemics in the United States about 75 per cent. The

mortality of the sporadic form has not been considerably lower, and has sometimes been higher. In making up the statistics on which this article is based they have excluded a certain number of cases. They exclude those cases which survive the first injection less than twenty-four hours. They think that it may be accepted as probable that any marked benefit which the serum may be assumed to exert could hardly be effectively manifested before this time. By this ruling they exclude 21 cases as moribund at the time of injection and 12 cases as fulminant. They also exclude 10 other cases which had secondary and intercurrent fatal complications, or which were chronically moribund, by which term is meant cases which were palpably dying at the time of the first injection, though they survived that first injection longer than twenty-four hours. Excluding these cases, there remain 393 cases; of these, 295 recovered, or 75 per cent. The best results were obtained in cases between five and ten years in age. At that age the mortality was only 11.4 per cent. In infants under one year the prognosis has been very bad, but there were 50 per cent. recoveries in 22 such cases of this series. Some discrepancy as to the higher mortality after twenty years of age exists, but there was not enough evidence to consider the prognosis worse at this age. Robb, of Belfast, treated 21 such cases. Of these, 18 recovered. Of the 3 cases that died, 2 were fulminant.

The histories of 361 cases were sufficiently accurate to enable the authors to approximate the period of the disease in which the first injection was made. The cases were nearly equally divided into three classes. The first class, in which the first injection was made in the first three days, gave a mortality of 16.5 per cent. The second class was injected from the fourth to the seventh day, and gave a mortality of 23.8 per cent. The third class, which includes all the cases injected after seven days, gave a mortality of 35 per cent. This shows that the earlier the injection is made the more favorable the prognosis. This is by no means an absolute rule, since there were many notable exceptions. These exceptions may be explained by individual factors of both patient and organism. The effects produced upon the meningococci in the spinal exudate were very striking. Very soon after the serum injections the diplococci tend to be greatly reduced in number, to disappear from the fluid part of the exudate, and to become wholly intracellular. They also present certain changes of appearance, a swelling and fragmentation, and are apt to stain irregularly. They also lose their viability in cultures. These changes may be due to some restriction of multiplying of the bacteria and to the greater phagocytosis of the leukocytes. Grossly, the spinal exudate loses its turbidity, at times very rapidly. Even distinctly purulent exudates cleared up entirely. Leukocyte counts made before and at regular intervals after the injections showed, in favorable cases going on to recovery, a fall in the number of the leukocytes in the circulating blood, which was often very rapid and even critical in character.

## PEDIATRICS.

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UNDER THE CHARGE OF

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**Pyopericarditis in Children under Twelve Years of Age.**—F. J. POYNTON (*Brit. Med. Jour.*, 1908, ii, 365) has studied 100 cases of pyopericarditis. Of these, 66 cases were less than three years old, 17 between three and four; males and females were affected alike. All of them had pulmonary disease as well, 60 having empyema, 40 pneumonia or acute pleurisy; a few also had acute pulmonary tuberculosis. Predisposing causes were measles, whooping-cough, and influenza; the exciting cause always the pneumococcus. From a pathological standpoint some had only a few flakes of fibrinopurulent exudate and a small amount of slightly turbid fluid; others had a fibrinoplastic exudate, similar to but softer than that in rheumatism; others had a large amount of creamy pus, and in the greater number a remarkable thickening of the pericardium was found with some inspissated pus and partial organization of the exudate. The pericarditis arises usually independently of the pleurisy by a simultaneous infection or secondary blood infection, and but rarely by direct continuity. In only 6 cases was the diagnosis confidently made. The difficulty of the diagnosis is due to the following: the pericardial friction exists but rarely; the patients are usually very young; pulmonary disease, such as pneumonia, pleurisy, or empyema, which may even be bilateral, always co-exists; there is no endocarditis; suppurative conditions in other parts of the body—meningitis, peritonitis—may also be present. An acute course was observed in 20 of the patients, in 50 a subacute, while the remainder ran a chronic course. In the first class the duration was about six weeks, in the last six months or longer. In the first class the disease usually began abruptly, in the second with cough, pleural pain, and wasting, in the third with gradual failure of health, strength, and wasting. The most important signs are progressive muffling of the heart sounds, enlargement of the cardiac area, dulness over the pericardium, pear-shaped outline of a distended pericardium, abrupt transition from dulness of fluid to resonance of lung tissue, and a wavy and diffuse pulsation to left of the sternum. The differential diagnosis from rheumatic pericarditis and the treatment are discussed. The latter must be surgical, and even then the disease is almost invariably fatal.

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**The Reappearance of a Cutaneous Reaction, which had already Disappeared, during a Scarlet-fever Infection.**—P. HEIM and M. K. JOHN (*Wien. med. Woch.*, 1908, lviii, 1831) report the case of a girl, aged four years, in whom von Pirquet's cutaneous reaction appeared in a most decided manner; the reaction disappeared at the usual time and was followed by four tuberculin injections for the purpose of treatment. Three days after the last injection, one month after the cutaneous reaction, the child broke out with the rash of scarlet fever and simul-

taneously with this the tuberculin papules reappeared; just at the time of the test there were three papules, and they appeared at exactly the same points. A little later at the points of the cutaneous injections, the dosage of which was extremely small, a local reaction also appeared at three places; this consisted of intense redness and infiltration, particularly at the last point of injection. The authors explain this in the following manner: The tuberculysins in the tuberculous child are attached originally to cells; at the onset of the scarlet fever they entered the circulatory stream at the same time as the scarlet fever antibodies; they dissolved the remains of the bacilli deposited in the skin and thus produced the second reaction.

**Pathogenesis of Whooping-cough.**—The publications of Bordet and Gengou concerning the etiology of whooping-cough led C. FRAENKEL to make a series of observations (*Munch. med. Woch.*, 1908, iv, 1683). The sputum of 38 patients was examined, but from only 8 of these could the characteristic organism be cultivated. All the positive cases were in the very beginning of the affection. The organism grew best on media containing considerable human blood. The bacillus is small in size, non-motile, does not stain after Gram stains in toto and quite evenly, and has a definite form even after a number of recultivations. It was obtained from all the early cases of whooping-cough. When pure cultures were injected into monkeys, and particularly when they were made to breathe air containing them, they developed a typical whooping-cough which lasted from eight to ten days; there was no expectoration. Inasmuch as the "Complementablenkung" was negative in four out of five tests, the agglutination test uncertain, and the organisms found in two children absolutely free from whooping-cough, Fraenkel feels that the position of this organism as the cause of whooping-cough is not firmly established; personally, however, he feels that the bacillus stands in some relation to the disease.

**Treatment of Scarlet Fever.**—K. OPPENHEIMER (*Munch. med. Woch.*, 1908, iv, 1691) discusses the treatment of scarlet fever with particular reference to baths and diet. He disagrees with the majority of the German authors, agreeing rather with French and American observers in regard to baths and cold sponging; he does not employ them unless the nervous system is affected. He considers their influence dangerous for the heart, and, more particularly through the possibility of taking cold, for the kidneys. Cold water, especially if applied in the form of packs, is almost certain to chill the kidneys and lead to nephritis. In the first stage of the illness his treatment is purely expectant; rest with plenty of water is probably all the child requires during this time; if the child does not wish to eat or drink he does not force food, but considers the rest more important. As soon as the child evinces some appetite milk is given, also diluted tea; later in the disease any food usually given a child is allowed, with the exception of meat, eggs, and their products. He emphasizes that none of the foods must be salted too much. He keeps his patients in bed for from five to six weeks; in the sixth week he permits warm bathing, using a 1 per cent. corrosive sublimate solution for the body. He has never seen a single kidney complication during the last eighteen years, although he has treated in that time more than 150 cases.

**Epidemic Infantile Paralysis.**—M. ALLEN STARR (*Jour. Amer. Med. Assoc.*, 1908, ii, 111) discusses the epidemic of acute anterior poliomyelitis occurring in New York and vicinity during the year 1907, in which over 2000 cases were observed. The epidemic began in May and lasted until December, being at its height during August and September. The mortality was 6 to 7 per cent. The summer was hot, but not unusually so; it was unusually dry, however. The onset of the disease was uniformly accompanied by brisk fever, vomiting, malaise, sweating, severe pains in limbs and back, rigidity of spine, and in a few cases retraction of head; diarrhoea lasted for a few days, and delirium began often about the second day. The paralysis was usually discovered about the third or fourth day. In the vast majority of cases the legs were chiefly affected, in some the arms as well, in some even the muscles of the back, abdomen, neck, face, and eye. True infantile hemiplegia, poliomyelitis with bulbar paralysis, poliomyelitis with polio-encephalitis of Wernicke, and the ordinarily recognized type of poliomyelitis were observed. Retention of urine and incontinence lasting for some days were observed, but in no case did either become permanent. Death was due to respiratory paralysis or heart failure, and not to the febrile affection. The paralysis was always flaccid, with rapidly following atrophy in the muscles and a rapid loss of faradic contractility. Pain in the affected parts was very common and frequently persisted. Many cases recovered absolutely; most of them improved very much. Bacteriological examination of the spinal fluid and of the blood, as well as serodiagnostic experiments were without result. The treatment consisted in dry-cupping or ice-bags in the early stage of the disease to relieve congestion; the fever could be kept down with sponging, or with coal-tar remedies, in suitable doses, with or without Dover's powder. To keep the patient quiet a purge should be given and the diet consist of milk. Urotropin is advised until the fever subsides because of its antiseptic properties. After the acute stage is over, strychnine, massage, and galvanism should be resorted to. Deformities should be prevented from the beginning of the condition.

**Skiagraphy of the Newborn.**—VAILLANT and BOUCHACOURT (*Ann. d. hygiène publique et de médecine légale*, 1908, ix, 65) have made a number of skiagraphic studies to determine whether it is possible to tell whether a dead child was dead at birth, whether it died shortly after, or some time after birth—with the following conclusions: (1) In children who have not lived at all no organs are visible on the skiagraph. (2) In children who made a few respirations the stomach alone is visible; the greater the number of respirations the clearer and larger is the picture of this organ; from the size of a small pea it becomes the size of a large bean. (3) In children who lived from one to fourteen hours the stomach picture is still clearer and larger; the intestine also became visible in the skiagraph. (4) In children who have lived several days without nourishment, more of the abdominal viscera become visible, and the lungs, which have not been permeable to the x-rays until this moment, become visible in the picture; the liver becomes sharply outlined, as well as the shadow of the heart, although the latter is not always so clear. (5) In children who have been fed for several days all the organs are more visible, and the gases contained in the intestines produce a better picture of the intestinal loops.

## OBSTETRICS

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**Rupture of the Uterus.**—HARTMANN (*Ztschr. f. Geburtshilfe und Gynäkologie*, 1908, 62) contributes a paper upon this subject, reporting four cases. The first was a multipara, whose child died during labor, and was delivered by craniotomy. When an effort was made to remove the placenta, a tear in the uterus was found giving access to the intestine. As there was no hemorrhage, and the patient's general condition was good when admitted to the hospital, no interference was practised, and she was treated entirely by the expectant method, with absolute rest and ice-bag upon the abdomen. She died on the fifth day from peritonitis, which developed so completely and suddenly that operation after its appearance was impossible. Autopsy showed a ruptured uterus with a bruised condition of the bladder wall, which was becoming gangrenous. The second patient had been delivered by embryotomy in a previous pregnancy. She had a contracted pelvis, and pubiotomy was proposed, but refused by the patient and her husband. Her suffering became so extreme that she consented to any operation, when her pain suddenly ceased and the temperature rose several degrees. On examination, rupture of the uterus was recognized. Abdominal section revealed a transverse tear above the cervix, extending widely into the right parametrium. The edges of the tear were not clean, showing that infection was present. The uterus was extirpated and the tissues brought together as well as possible. Gauze packing was introduced, which was brought down through the vagina, and the vaginal wound was closed. The patient suffered shock on the evening of the operation, and had considerable abdominal distention during convalescence. The tissues on the right side of the uterus became infected by *Bacillus coli communis*; pus formed and was evacuated above Poupart's ligament. The patient finally recovered.

In Case III it was determined to open the pelvis and then wait for spontaneous labor. As the head entered the upper pelvis, labor was proceeding well, no operation was done, when, without warning, a moderate hemorrhage occurred from the vagina. The child's heart sounds immediately fell to 100, then to 80, and then ceased. The mother complained of no pain and had a normal pulse of 70. Smaller foetal parts could be felt at the umbilicus. The child was delivered with forceps, with the occiput posteriorly, but an effort to deliver the placenta failed without the introduction of the hand. It was then observed that the upper portion of the uterus was torn completely across, and that coils of intestine were lying in the uterine cavity. The uterus was then removed through the vagina. The patient made an uninterrupted recovery without complications. This patient had previously been delivered by Cesarean section by the transverse incision of Fritsch. Rupture of the uterus occurred in this scar. Microscopic examination of the uterine tissues at the point



of rupture showed that after the original operation the different layers of the uterus had not accurately united. In some portions only the serous covering was joined; a very thin sheet of muscular tissue accompanied the serous covering at these points.

The fourth case was a multipara, who had been delivered by craniotomy, and who also had had spontaneous births. The patient was brought to the hospital in a wagon, having been delivered by a physician by forceps, after version had failed. He had diagnosed rupture of the uterus after delivery. A laceration in the anterior portion of the vagina and cervix, extending into the uterus, could be recognized. The uterus was removed through the vagina and an ovarian cyst was found upon the right side, which was also removed. There had been free hemorrhage into the abdomen and a collection of blood upon the left side in the broad ligament. The bladder was not wounded. The patient made a tedious recovery. Microscopic examination of the tissues of this uterus showed degeneration of its muscular fiber.

Hartmann has collected 18 cases of rupture of the uterus in the scar of a previous Cesarean section. In some of these the placenta was attached at the point of rupture, and in others the histories stated that involution proceeded with great rapidity. These cases seem also peculiar in that the patient complained of very little pain at the time of rupture, and seemed much less disturbed than in cases in which rupture occurred without section. It cannot be ascertained that any one suture material is more unreliable than any other in this regard; in some of these the muscle had been closed by silk, in others by catgut. As regards the treatment of rupture of the uterus by vaginal extirpation, Hartmann has collected 29 cases, with a percentage of recovery of 51.7 and mortality of 48.3. Eversmann's collection of 71 cases, treated by use of the tampon, shows a percentage of recovery of 59 and a mortality of 41. Hartmann considers vaginal extirpation of the ruptured uterus an especially valuable operation. When rupture occurs in general practice, he would have the attending physician, if possible, remove the child and tampon the uterus and vagina. This should control the hemorrhage. He would then have the patient transferred, as soon as possible, to the nearest hospital. In cases in which the child cannot be safely delivered through the vagina, he would remove it by abdominal section, removing the uterus by vaginal section.

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**The Supports of the Pelvic Viscera.**—PARAMORE (*Jour. Obst. and Gynec. British Empire*, September, 1908) contributes a paper, which he has enlarged somewhat from his previous writings upon this subject. He believes that variations in abdominal pressure are of the greatest importance in determining prolapse of the pelvic viscera. He also believes that firm contraction of the levator ani muscle is of great importance in preventing the prolapse or expulsion of pelvic contents. He draws attention to the clinical value of rest in bed in preventing prolapse.

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**Purulent Infection of the Uterus by Bacillus Coli Communis.**—WHITEFORD (*Jour. Obstet. and Gynec. British Empire*, September, 1908) describes the case of a patient who had an apparently spontaneous labor, followed, three weeks afterward, by a chill with pain in the abdomen. There was a central abdominal tumor, slightly tender, very tym-

panitic, midway between the pelvis and the umbilicus. The tumor was increasing in size. On dilating the cervix a quantity of very foul pus and gas escaped. The pus was dark brown in color, and the odor suggestive of infection with *Bacillus coli communis*. Under repeated irrigation with peroxide of hydrogen, the odor disappeared, but the patient became rapidly worse, and died, with extensive alterations in the blood. *Bacillus coli communis* was found in great abundance in the tissues. The examination of the uterus showed that there was an infected fibroid in the body of the uterus, and that the cervix was infected and occluded with masses of pus.

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**Cancer of the Breast Complicating Pregnancy.**—CHEYNE (*Brit. Med. Jour.*, October 3, 1908) contributes a paper upon cancer of the breast and its treatment, in which he states that in comparatively young women during pregnancy or lactation diffuse carcinoma is occasionally seen, and that it grows so rapidly that it resembles subacute mastitis. The skin becomes infiltrated and swollen, and the glands in the axilla are usually involved in an early stage of the disease. These cases proceed so rapidly that surgical treatment is usually of little avail when the patient comes under observation.

[The reviewer can confirm this observation by a recent case in which, in a second pregnancy, a diffuse and highly malignant carcinoma developed from the site of a small tumor removed after the first pregnancy. The physical appearances were those of diffuse mastitis, and the patient, a convert to Christian Science, would not permit interference of any sort. Finally, her pain became so great that surgical aid was sought, and the fluctuating portion of the breast opened under ether; straw-colored fluid escaped, and pieces of tissue were removed for examination. This was found to be encephaloid carcinoma of the most violent type. The patient succumbed from the disease within a few weeks.]

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## GYNECOLOGY.

UNDER THE CHARGE OF

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**The Epithelium in the Mature Uterus.**—L. MANDL (*Zentralbl. f. Gynäk.*, 1908, xxxii, 425) concludes from the results of his histological studies that the epithelium of the endometrium is not always ciliated, and that when cilia are present there are nevertheless here and there areas in which the epithelium is nonciliated. In animals the periods in which the epithelium is ciliated are of very short duration. Among the ciliated epithelial cells of the Fallopian tubes there are numerous nonciliated secretory cells. At such times, as the uterine epithelial cells normally ciliated are devoid of cilia, they seem to exercise a secretory function.

**The Significance of Pain in Pelvic Disease.**—EMIL NOVAK (*Amer. Jour. Obst.*, 1908, lvii, 473) suggests that while it is true that a careful physical examination is of the first importance in the diagnosis of pelvic disorders, yet a consideration of the character and distribution of the pelvic pain will often yield interesting and suggestive information, although the limitations of such observations from the standpoint of diagnosis are evident. The good surgeon will endeavor, as far as possible, to ascertain the exact nature of the disease before resorting to operation, and will not rest content with merely deciding as to the advisability or inadvisability of operation. The pain of pelvic visceral disease is, in a general way, governed by the same laws which apply to the causation of pain in the other abdominal viscera. One of the dangers of neglect of pelvic disease is the possibility of the development of a condition of neurasthenia, with a diffusion of pain to other parts of the body, and the appearance of other more or less characteristic symptoms of this condition. One of the reasons for the continuance of unpleasant symptoms after operative treatment of pelvic lesions, is the persistence of the neurasthenia which is frequently a complicating factor in such cases. Hysteria, as it manifests itself by pelvic symptoms, presents the same characteristics which distinguish it as it appears in the other parts of the body. The removal of normal ovaries for conditions of pelvic pain is founded upon an erroneous and obsolete conception of the mechanism of such pain, and modern surgery has condemned such a procedure as unjustifiable from a theoretical point of view, and useless from the standpoint of clinical experience. The so-called fibrocystic ovaries are frequently found in women who enjoy perfect health, and hence great caution is necessary in attributing pelvic pain to such organs. If operative treatment be resorted to at all, it should be conservative rather than radical. The gynecologist must learn to look upon pain as the resultant of two factors, the lesion and the patient, and in order to arrive at an intelligent appreciation of the true significance of pelvic pain he must study both these factors with equal fidelity.

**The Treatment of Cancer of the Female Genital Organs.**—J. L. FAURE (*An. de gyn. et d'obst.*, 1908, v, 335) in a report of his work compares the different surgical operations for cancer of the cervix and greatly prefers the broad abdominal operation, following practically the operation known as Wertheim's, which was planned by Emil Ries, of Chicago. Faure considers isolation of the ureters in the broad ligament a very important essential, and removal of any enlarged glands as well as the aggregation of glands at the iliac bifurcation important, although opposed to attempts at removal of all pelvic lymph glands and all the connective tissue between the uterus and the pelvic wall.

**Ventrosuspension an Unsafe Operation for Posterior Displacement of the Uterus during the Child-bearing Age.**—E. B. CRAGIN (*Surg., Gyn., and Obst.*, 1908, vii, 45) says the forms of dystocia after too firm attachment, which are most commonly noted, are: (1) A malpresentation of the child, especially a transverse presentation. This transverse presentation was noted in 15 of the 21 cases of Cesarean section for this condition collected by Lynch, and occurred in all 5 of the cases operated on by Craigin and here reported. (2) An ineffectual labor with cervix un-

dilated and high up. This high position of the cervix is noted in most of the cases demanding Cesarean section, and was present in all of his cases. (3) An unobstructed labor, the obstruction being produced by the thickened anterior uterine wall. Cragin insists that ventrosuspension is not safe in child-bearing women, as it may become a fixation instead of a suspension in one or the other of the following ways: The area of adhesion between the uterine fundus and the abdominal wall may be broader than expected, and the resulting band be too firm to allow uterine mobility. Infection of the abdominal wound may fix the fundus and anterior uterine wall firmly to the abdominal wall. A ventrosuspension, which allows a normal delivery in the first pregnancy following operation, may subsequently become a ventrofixation and produce dystocia so marked as positively to indicate Cesarean section in the second post-operative pregnancy. Cragin reports briefly histories of 5 Cesarean sections he has done as a result of these operations.

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**The Supports in Chief of the Female Pelvic Viscera.**—R. H. PARAMORE (*Jour. Obst. and Gyn., Brit. Emp.*, 1908, xiii, 391) has a carefully prepared article on this subject, and seeks to prove that the pelvic floor is the structure chiefly concerned in holding these organs in proper position. Paramore insists that it is evident that the pelvic viscera are maintained in their position by two sets of forces: one acting from above and pinning, so to speak, the viscera in their places and known as intra-abdominal pressure. The other acts from below, supports the viscera, and prevents their being displaced by any excessive force from above. These two forces, therefore, vary directly with each other; increase of one produces reflexly an increase of the other. This mechanism is under nervous control, which determines any desired end (coughing, defecation, etc.). The force from below is principally supplied by the levator ani and is the essential element in maintaining the normal visceral position. When the pelvic floor is inhibited during defecation, the visceral connective tissue is capable of supporting the viscera temporarily, but is not capable of more than this. When the muscle has become insufficient this connective tissue is unable to maintain the viscera in position.

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**The Pathology and Operative Treatment of Displacements of the Pelvic Viscera.**—W. E. FOTHERGILL (*Jour. Obst. and Gyn., Brit. Emp.*, 1908, xiii, 410) has written extensively and dogmatically upon the pathology and operative treatment of displacement of the pelvic viscera, his recommendations being based upon his conception of the supports of the pelvic viscera as portrayed in his paper in the same journal in January, 1908. He regards classical prolapse of the pelvic viscera (descent of the uterus and its appendages with the bladder, the urethra, and the vagina) as being due to prolongation of the perivascular connective tissue, in the base of the broad ligaments, which extends laterally up to the internal iliac arteries, and that such elongation gives rise to a relaxation that can never be removed. Fothergill, therefore, thinks that surgical treatment is necessarily limited to plastic surgery of the vagina, the perineum, and the cervix uteri, plus ventrofixation. He believes that a part only of the elongation mentioned may exist, which would cause descent of the bladder and the anterior vaginal wall. In some

instances descent of the posterior wall of that canal may also result. In cases of relaxation, as just mentioned, only the lower portion of the mass supporting the uterus is affected, the upper part preserving its function, and the treatment being only plastic surgical procedures. Again, Fothergill regards retroversion or retroflexion of the uterus as being due to the same character of elongation and resulting relaxation occurring in the upper part of the pelvic viscera. When surgical treatment is needed he recommends Alexander's operation when the uterus is movable, and if adhesions or diseased appendages exist, laparotomy, with appropriate treatment of these complications, and Webster's round ligament operation. Apparently no instance of unusual elongation of the uterus with recurrence of prolapse has been noted by him, although others occasionally find them.

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## DERMATOLOGY.

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**The von Pirquet Cutaneous Tuberculin Inoculation.**—KÖNIG (*Archiv f. Dermat. u. Syphilis*, 1908, lxxxix, Heft 3), who inoculated 20 patients with lupus with the old tuberculin according to the method of von Pirquet, obtained reactions varying from the mildest erythema with a scarcely demonstrable infiltration to deep subcutaneous, extremely painful nodules with lymphangitis. All these disappeared, some quickly, some slowly, with scaling and pigmentation. In one case, in which, in addition to an extensive lupus, there were clear signs of pulmonary disease, a general reaction occurred accompanied by severe headache, vomiting, and chills. In 2 cases a conjunctivitis followed the inoculations. The strength of the reaction in the sound skin appeared to depend very much upon the severity of the lupus, those with extensive disease showing a much stronger reaction than those in whom a small area was affected. König believes, from his clinical experience with these inoculations, and from histological study of the lesions resulting from them, that they may be employed, not only for diagnostic purposes, but therapeutically. As to whether the lesions produced by these inoculations are actually tuberculous he does not venture to give a positive opinion, but he inclines to the view that they are non-tuberculous.

**Kraurosis Vulvæ.**—THIBIERGE (*Ann. de dermat. et de syphil.*, 1908, No. 1), in a recent clinical study of this interesting and but little understood affection of the female genitalia, finds nothing to support the belief that it may follow leukoplakia of the vulva. The distressing itching

which sometimes accompanies the affection he regards as a mere coincidental symptom and not as a necessary part of it. He is inclined to believe that the disease is present to a greater or less degree in all elderly or old women, and is not dependent upon local causes, such as blenorrhœa, sexual excess, or syphilis. He concludes his study as follows: Kraurosis vulvæ, characterized at its acme by a greater or less constriction of the vulvar orifice, by atrophy and a peculiar smoothness of the integuments of the vulva with loss of their elasticity, is preceded by a longer or shorter period during which smoothness and atrophy of the vulvar mucous membrane exist without appreciable contraction of the vaginal orifice. It is the result of the involution of the tissues about the orifice of the vulva, and is connected with the suppression of the function of the ovaries.

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**Dermolysis.**—C. J. WHITE (*Jour. Cut. Dis.*, July, 1908), under the above title, reports a case of a hitherto undescribed affection of the skin. The disease, which occurred in a Russian, aged twenty-five years, was characterized by an eruption of cherry-colored papules about the size of a pea limited to the elbows and suprapatellar regions of the thighs. The lesions after a time flattened out or were depressed in the centre, became softer than the new ones, and changed to a muddy-white color. Histologically there were noted "conspicuous epidermal changes; endarteritis; perivascular, perifollicular, and periglandular lymphocytic infiltration; basophilic collagen; collastin, general diminution of collagen and elastin; and, lastly, gradual disappearance of all these structures focally." White has been unable to find any similar condition reported in literature.

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**Further Experience with the White and Blue Light of the Quartz Lamp.**—KROMAYER (*Jour. Cut. Dis.*, June, 1908) finds that the undesirably strong superficial action of the quartz lamp may be obviated by the addition of a solution of methylene blue to the water-bath of the lamp. He believes that the light from this lamp is more penetrating than that from the Finsen apparatus, although he admits that other experimenters have not confirmed this. This light has been successfully employed in the treatment of lupus vulgaris, lupus erythematosus, chancroid, telangiectasis, nævus vascularis, acne rosacea, acne vulgaris, furunculosis, folliculitis barbæ, folliculitis decalvans, eczema, psoriasis, alopecia areata, and ulcus cruris. In lupus vulgaris, vascular nevus, and alopecia this treatment succeeds better than any other yet employed.

SCHMIDT (*Dermat. Zeit.*, April, 1908), who has treated 20 cases of lupus vulgaris with the Kromayer quartz lamp, does not regard it as an efficient substitute for the Finsen apparatus. While absorption of a great part of the lupus tissue may be produced by the light, it soon loses its efficiency, leaving lupus nodules still present. He does not find that the use of methylene blue solution prevents the undesirable superficial necrosis which frequently follows the use of the lamp.

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**A Vacciniform Drug Eruption.**—VÖRNER (*Dermat. Zeit.*, 1908, xv, Heft 6) reports a case of vaccine-like eruption following the use of antipyrine and salicylic acid. The patient was a man, aged sixty-three years, who suffered from a right-sided thoracic zoster, for which he was given

0.5 gram each of antipyrine and salicylic acid three times a day. After taking the fourth powder the patient experienced marked itching, which lasted but a short time, and was followed by a more or less general eruption of discrete vesicles the size of a hemp seed to a lentil, many of which showed a central umbilication; there was no fever nor were there any subjective symptoms.

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**A New Method of Treating Lupus Erythematosus.**—HARTIGAN (*Brit. Jour. Dermat.*, March, 1908), at a meeting of the Dermatological Section of the Royal Society of Medicine, exhibited 5 cases of erythematosus lupus which he had treated by applications of a 2 per cent. solution of zinc or copper sulphate. The cases were of the circumscribed variety, presenting the sebaceous and telangiectatic type, and had lasted from fifteen months to twelve years. In one of the cases the eruption had entirely disappeared, while in the remaining 4 but few traces of the disease were left. Prompter and more satisfactory results had been obtained by this treatment than by any other.

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**Albuminuria in Scabies.**—NICHOLAS and JAMBON (*Ann. de dermat. et de syphil.*, 1908, No. 2), in a series of 100 cases of patients with scabies, found albuminuria sixteen times. From their study of the literature and from their own observations they conclude that scabies is frequently accompanied by albuminuria, which in its appearance, duration, and disappearance is essentially dependent upon the cutaneous lesions which have given rise to it. Besides the physiological and medicamentous albuminurias, and the albuminuria due to previous Bright's disease, which one may meet in scabies, there is undoubtedly a true albuminuria arising from the evolution of the acarus in the skin. This scabious albuminuria may present itself under two clinical types: (1) Simple, scabious albuminuria, so called without any subjective or objective symptoms, a chance clinical finding, disappearing rapidly after treatment of the scabies, due perhaps to a slight nephritis; (2) true scabious nephritis, with a more or less complete train of the classical symptoms of acute, subacute or chronic nephritis, disappearing with the scabies, or persisting after the cure of the dermatosis. The albuminuria of scabies does not seem to be due to any single cause nor to arise from the single lesion. Sometimes it is a true toxic nephritis, more or less marked and profound; sometimes it arises from the cutaneous irritation alone, being due to reflex modification of the renal circulation or of the functions of the renal epithelium.

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**Radiotherapy in the Treatment of Acne Keloid.**—KIENBÖCK (*Archiv f. Dermat. u. Syphilis*, 1908, xc, Heft 3) reports 4 cases of that very disfiguring and obstinate affection, acne keloid (dermatitis papillaris capillitii of Kaposi) successfully treated by means of the x-rays. Kienböck finds that radiotherapy produces prompt healing even in cases which have lasted many years; in some instances a single sitting may be sufficient to bring about the disappearance of the disease. He advises the use of moderate or large doses.

## HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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**Vaccination against Typhoid Fever, Cholera, and Pest**—It will be remembered that Wright some years ago introduced vaccination against typhoid fever in the British Army. At the outbreak of the Boer war a considerable number of troops had been vaccinated, and it was hoped that the medical record of that campaign would supply definite information concerning the value of this prophylactic measure. But there were so many disturbing factors influencing the health of the troops and the hospital records, that this hope was not realized. At the close of the South African War vaccination against typhoid fever was discontinued among British soldiers, but later it was taken up again and referred to a commission. LEISHMAN (*Berichte über den XIV Internationalen Kongress f. Hygiene und Dermographie*, ii, 536) has made a preliminary report upon the work and observations of this commission. The vaccine consists of cultures of the typhoid bacillus in meat and broth. These are sterilized, when from twenty-four to forty-eight hours old, at a temperature of 53°, maintained for one hour. The strains used are old, and are possessed of but slight virulence. These sterilized cultures are preserved by the addition of 0.25 per cent. of lysol, and are standardized by an enumeration of the number of bacteria in a given volume of the vaccine. When possible two inoculations are made, the first of 500,000,000, and the second of 1,000,000,000 bacteria, with an interval of ten days. This means, as a rule, 0.5 c.c. for the first and 1 c.c. for the second injection. The site of the injection is either the pectoral region or the outer surface of the upper arm at the insertion of the deltoid. The inoculations are made in the afternoon, and as a rule those treated are returned to duty on the second day afterward. The results of these inoculations in seven large Indian stations during the six months from January 1 to June 30, 1907, are shown in the following table:

	Mean strength.	Cases.	Deaths.	Incidence per 1000.	Mortality per 1000.
Non-inoculated . . . . .	8113	173	42	21.32	5.18
Inoculated . . . . .	2207	15	3	6.80	1.36

MUSEHOLD (*Ibid.*, 545) reports upon typhoid fever vaccination in the German army. The German vaccine is prepared by adding a normal loop (2 mg.) to each 0.5 c.c. of normal salt solution, and this is sterilized at 60°. Three inoculations are made. At first these consisted of 0.5, 1, and 1.5 c.c. of the vaccine, or 1, 2, and 3 loopfuls of the agar culture, but the reactions that followed these treatments were in some instances so serious that the dose was diminished and those now given are 0.4, 0.8, and 1.2 c.c.

The symptoms that follow these inoculations are fairly uniform. Within a few hours there is a chill, followed by fever and vomiting.



The temperature may go as high as 41°, though generally not more than 40°, and this is accompanied by albuminuria and cylindruria. The use of alcohol following the inoculation is forbidden, as it has been found to intensify and prolong the symptoms. Among more than 8000 vaccinated no lasting harm has been observed. Only those who are willing to do so are submitted to these preventive inoculations. The results of these inoculations seem to be beneficial, as shown by both the morbidity and mortality reports. The number of cases per thousand among the inoculated is 98.4. The beneficial effect on the course of the disease is shown by dividing the cases into (1) the fatal, (2) the severe, (3) the moderate, and (4) the light, such grouping showing the following:

In the inoculated per thousand . . . . .	3.3 : 8.9 : 13.2 : 25.5
Or as . . . . .	1 : 2.7 : 4.0 : 7.7
 In the uninoculated per thousand . . . . .	 12.6 : 25.4 : 24.4 : 36.2
Or as . . . . .	1 : 2.0 : 1.9 : 2.9

STRONG (*Ibid.*, 1085) finds that vaccination with dead pest bacilli or with bacillary extracts gives practically no immunity in the lower animals, and he is using in Manila a living non-virulent culture. In experimental animals these inoculations induce a fair degree of immunity, and in a small epidemic the deaths among the inoculated was 66.6 per cent., while among the vaccinated it was only 16.6 per cent. However, the number of the vaccinated exposed in this epidemic was too small to justify any positive conclusions. The size of the dose employed is one suspended twenty-four-hour agar start for adults, and from one-third to one-half this quantity in children. Strange to say, injections of these large amounts cause no severe reactions. The fact that the culture remains avirulent is determined from time to time by animal tests. Experiments on monkeys show that the avirulent pest bacilli are found quite abundantly in the tissue about the point of inoculation for from six to eight hours, after which time they gradually diminish, and after twenty-four hours they are seldom detectable. Strong holds that his method of inoculation for pest is a true vaccination, "the organism reproducing itself in the tissues for probably one hundred or more generations, and its successive groups of receptors stimulating the production of corresponding groups of amboceptors in the animal body."

In inoculating against cholera Strong injects 1 c.c. of the extract from virulent bacteria made according to the methods of Brieger and Neisser and of Shiga and Wassermann. He has treated over 6000 people by this method, and concludes that from a single inoculation a higher immunity can be obtained by this prophylactic than by any other.

PFEIFFER (*Ibid.*, 1071) discusses vaccination against typhoid fever, pest, and cholera. In the first place he speaks of the preparation of the vaccine. He states that not every culture is suitable or this purpose. In order to have a good cholera vaccine it is necessary to have a highly virulent culture. With typhoid fever the question of suitability of the culture is much more complicated, for, as Wassermann says, it is not the virulence of the culture so much as the affinity of the bacilli for the specific amboceptors that must be regarded as the determining factor; therefore the preferable culture is the one that absorbs from an immune serum the greatest amount of the anti-bodies. This can be determined

only empirically on either men or animals, and the culture that induces the most marked specific changes in the blood should be selected. It is probably better still to employ a culture of mixed strains. The vaccine of Pfeiffer and Kolle is prepared by adding the growth on agar cultures to physiological salt solution and sterilizing at 60°; that of Wright by sterilizing young cultures at 60° (this has been changed by the commission, as has been stated, to heating for one hour at 50°); that of Löffler by drying the cell substance at from 120° to 150°; that of Macfayden and Rowland by rubbing up or grinding the bacilli at the temperature of liquid air; that of Neisser and Shiga, also that of Wassermann, by sterilization at 60°, and subsequent autolysis for five days at 37.3°; when the culture is filtered through porcelain, after which the filtrate may be used directly (method of Neisser and Shiga), or it may be evaporated in vacuo and the dry residue employed (the method of Wassermann); that of Brieger, Conradi and Meyer, by suspending the living bacillus in distilled water, shaking vigorously for three days, and filtering through porcelain. Pfeiffer is inclined to the belief that the dose of the vaccine should be large enough to induce slight toxic effects. Subcutaneous injections are safer than intravenous ones, and in most instances the former are preferable, although a higher degree of immunity may be obtained with smaller doses intravenously. Two or three inoculations at intervals of from five to eight days are recommended as preferable to single ones. For typhoid fever, Löffler seeks to induce local intestinal immunity by long-continued administration of dead bacilli per os, and he has succeeded by this method experimentally in immunizing field mice to mouse typhoid. The possibility of developing a negative phase by vaccination is a question of the greatest importance. Pfeiffer is inclined, from his experimental work on animals, to deny that vaccination is followed by a negative phase, but he is cautious in his statements on this point. The work of Bail with his aggressins and that done with the typhoid residue in this country, certainly suggest the possibility of using the vaccine in too large doses; however, this would be much less likely to happen with the insoluble germ substance than with the soluble aggressins and residues. But the latter must prove to be the more suitable vaccines on account of their solubility, their ready diffusibility, and because they induce no toxic effect. It seems that even the most scientific men are slow to believe that any protective or curative agent can be of service to the body unless its administration is followed by some recognizable toxic effect.

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